

Study Title
COMBINED CHRONIC TOXICITY/ONCOGENICITY
STUDY 2-YEAR ORAL GAVAGE STUDY IN RATS

Laboratory Project ID:

Volume 2 of 13

NUMBER OF PAGES IN VOLUME: 245

- TEST GUIDELINES:**
- U.S. EPA Health Effects Test Guidelines OPPTS 870.4300 Combined Chronic Toxicity/Carcinogenicity (1998)
 - OECD Guidelines for the Testing of Chemicals Section 4 (No. 453) Health Effects (2009)
 - JMAFF Japan Agricultural Chemicals Regulation Law 12 Nousan No. 8147 (2000)
 - EEC Methods for the Determination of Toxicity Method B.33 Combined Chronic/Carcinogenicity test, Directive 88/302/EC (1988)

AUTHOR:

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Appendix D
Individual Detailed Clinical Observations

On occasion, clinical findings may have been observed more than once during the interval and were recorded accordingly. The individual clinical observations table of this appendix reports the findings observed, not the number of times observed.

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>0 mg/kg/day</u>	
1001 No abnormalities detected	1-52
1002 No abnormalities detected	1-52
1003 No abnormalities detected Teeth cut	1-39, 42-52 40, 41
1004 No abnormalities detected	1-52
1005 No abnormalities detected	1-52
1006 No abnormalities detected	1-52
1007 No abnormalities detected Abrasion(s), Cervical region Hair sparse, Cervical region Scabbed area, Cervical region	1, 13-52 2-4 7-12 5, 6
1008 No abnormalities detected	1-52
1009 No abnormalities detected Hair sparse, Axillary region/left Hair sparse, Axillary region/right	1-19 52 52

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>0 mg/kg/day</u>	
1009	31
Hair sparse, Cervical region	20-51
Hair sparse, Thoracic region	
1010	1-52
No abnormalities detected	
1011	1-97
No abnormalities detected	101
Hair wet, Anogenital region	98-103
Skin discolored, Brown, Tail	
1012	1-43
No abnormalities detected	58
Feces soft	44-68
Hair sparse, Cervical region	51-90
Nodule, 1-5 mm, Lip	
1013	1-92
No abnormalities detected	93, 94
Swelling, Axillary region/left	
1014	1-59
No abnormalities detected	60-103
Nodule, 5-20 mm, Tail	
1015	1-4, 16-96, 98-103
No abnormalities detected	5-15
Hair sparse, Forefoot/left	5-15
Hair sparse, Forefoot/right	97
Hypersensitive to touch	

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>0 mg/kg/day</u>	
1015 Vocalization	97
1016 No abnormalities detected	1-68, 71-83
Activity decreased	86
Carriage low	86
Hair discolored, Yellow, Ventral surface	84-86
Material around nose, Red	86
Nodule, 1-5 mm, Sacral region	86
Posture hunched	85, 86
Swelling, Thoracic region	69, 70
Thin	85, 86
1017 No abnormalities detected	1-14, 31-69
Hair sparse, Face	15-30
Scabbed area, Face	15
1018 No abnormalities detected	1-60, 63-66, 68-78
Material around nose, Red	61, 62
Swelling, Hind foot/left	67, 79-93
Swelling, Hind foot/right	79-93
Ulcer plantar/palmar, 5-20 mm, Hind foot/left	89-93
Ulcer plantar/palmar, 5-20 mm, Hind foot/right	89-93
Vocalization	89-93
1019 No abnormalities detected	1-68, 72-74

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>0 mg/kg/day</u>	
1019	Activity decreased 75-78
	Breathing slow 75-78
	Swelling, Thoracic region 69-71
	Thin 78
1020	No abnormalities detected 1-28, 43-77
	Hair sparse, Thoracic region 29-42
1021	No abnormalities detected 1-52, 55-96
	Carriage low 98
	Hair wet, Abdominal region 97, 98
	Limb function impaired, Hind limb/left 98
	Limb function impaired, Hind limb/right 98
	Swelling, Cervical region 53, 54
	Swelling, Hind foot/left 98
	Swelling, Hind foot/right 98
	Swelling, Nose/muzzle 53, 54
1022	No abnormalities detected 1-94
	Eye protruding, Eye/left 95-99
	Eye protruding, Eye/right 95-99
1023	No abnormalities detected 1-86
	Teeth cut 87

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number		Week(s) Sign Present
<u>0 mg/kg/day</u>		
1024	No abnormalities detected	1-66, 69-91
	Hair discolored, Yellow, Anogenital region	92
	Piloerection	92
	Posture hunched	92
	Swelling, Hind foot/left	67, 68
	Thin	92
1025	No abnormalities detected	1-6, 26-38, 91-96
	Hair discolored, Brown, Face	97-103
	Hair discolored, Brown, Ventral surface	103
	Hair sparse, Forefoot/left	7-24, 39-81
	Hair sparse, Forefoot/right	7-25, 39-81
	Material around nose, Black	63, 64
	Material around nose, Brown	101-103
	Material around nose, Red	72-88
	Penis extended	89, 90
	Swelling, Prepuce	89, 90
	Unkempt appearance	97-103
1026	No abnormalities detected	1-101
	Posture hunched	102, 103
1027	No abnormalities detected	1-4, 46-60

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Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>0 mg/kg/day</u>	
1027	Head tilt 61, 62
	Malocclusion 10-45, 61, 62
	Teeth broken 7-11
	Teeth cut 5, 6, 15-19, 61, 62
1028	No abnormalities detected 1-58, 63, 64, 69
	Feces soft 89-91
	Hair discolored, Yellow, Anogenital region 70-91
	Lacrimation, Eye/right 85-89
	Material around eyes, Black, Eye/right 82, 83, 85-88
	Material around eyes, Red, Eye/right 65-68, 89-91
	Nodule, 1-5 mm, Dorsal surface 59-62
	Scabbed area, Dorsal surface 59-62
1029	No abnormalities detected 1-96
	Abrasion(s), Anogenital region 103
	Material around nose, Brown 97-102
1030	No abnormalities detected 1-31, 42-85
	Hair sparse, Axillary region/right 32-41
1031	No abnormalities detected 1-88, 91
	Activity decreased 103
	Carriage low 102, 103

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>0 mg/kg/day</u>	
1031	103
Hair discolored, Brown, Anogenital region	92-103
Hair sparse, Anogenital region	97-103
Hair wet, Abdominal region	89
Penis extended	89, 90
Swelling, Prepuce	98-103
Swelling, Thoracic region	97-103
Unkempt appearance	
1032	1-19
No abnormalities detected	20-65
Hair sparse, Face	
1033	1-42
No abnormalities detected	
1034	1-60
No abnormalities detected	61-63
Unkempt appearance	
1035	1-83
No abnormalities detected	84-103
Hair discolored, Brown, Dorsal surface	89-103
Hair discolored, Brown, Ventral surface	95-103
Nodule, 1-5 mm, Dorsal surface	89-103
Piloerection	97-103
Unkempt appearance	89-91
Vocalization	
1036	1-86
No abnormalities detected	

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Individual Detailed Clinical Observations - MALE

Group, Animal Number		Week(s) Sign Present
<u>0 mg/kg/day</u>		
1036	Eye discolored, Pale, Eye/left	97-103
	Eye discolored, Pale, Eye/right	97-103
	Hair discolored, Brown, Abdominal region	89-103
	Hair discolored, Yellow, Abdominal region	87, 88
	Posture hunched	101-103
1037	No abnormalities detected	1-7, 53-67
	Eye discolored, Cloudy, Eye/left	86-89
	Eye discolored, Cloudy, Eye/right	86-89
	Hair discolored, Brown, Ventral surface	68-89
	Hair sparse, Cervical region	14-52
	Hair wet, Ventral surface	89
	Nodule, 1-5 mm, Hind foot/right	80-88
	Scabbed area, Cervical region	14-19
	Scabbed area, Face	8-13
	Ulcer plantar/palmar, 1-5 mm, Hind foot/right	89
1038	No abnormalities detected	1-5, 36-67
	Hair sparse, Cervical region	6-11
	Hair sparse, Forefoot/left	10-35
	Hair sparse, Forefoot/right	10-28
1039	No abnormalities detected	1-19, 91-96
	Hair sparse, Anogenital region	29, 30

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Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>0 mg/kg/day</u>	
1039	Hair sparse, Forelimb/left 20-90
	Hair sparse, Forelimb/right 20-90
	Hair sparse, Shoulder/left 25-37
	Hair sparse, Shoulder/right 31-37
	Hair sparse, Thoracic region 25-62
	Head tilt 99-101
	Material around eyes, Black, Eye/left 82-89
	Posture hunched 97-101
	Scabbed area, Shoulder/right 73, 74
	Skin discolored, Brown, Tail 97-101
	Unkempt appearance 98-101
	Vocalization 89
1040	No abnormalities detected 1-94
1041	No abnormalities detected 1-88, 90-97, 100-102
	Discharge, Red, Penis 98, 99
	Piloerection 103
	Vocalization 89
1042	No abnormalities detected 1-55, 59-88
	Discharge, Red, Penis 56-58
	Swelling, Hind foot/left 89
1043	No abnormalities detected 1-76

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Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>0 mg/kg/day</u>	
1044	No abnormalities detected Scabbed area, Face Swelling, Digit
	1-7, 12-43 8, 9 10, 11
1045	No abnormalities detected Hair sparse, Face Hair sparse, Forefoot/left Hair sparse, Forefoot/right Hair wet, Anogenital region Hypersensitive to touch Vocalization
	1, 29, 30, 82, 83, 86-101 2-28 25, 31-81 25, 31-81 102, 103 84, 85 84, 85
1046	No abnormalities detected Hair sparse, Forefoot/left Hair sparse, Forefoot/right Scabbed area, Cervical region
	1 2-27 2-27 27
1047	No abnormalities detected Hair sparse, Face
	1-5, 10-68 6-9
1048	No abnormalities detected Posture hunched Thin
	1-52 53, 54 53, 54

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Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>0 mg/kg/day</u>	
1049	No abnormalities detected Swelling, Axillary region/right Unkempt appearance
	1-65, 71-83 66-70 84, 85
1050	No abnormalities detected Nodule, 1-5 mm, Thoracic region
	1-83 84, 85
1051	No abnormalities detected
	1-91
1052	No abnormalities detected Hypersensitive to touch Swelling, Thoracic region Vocalization
	1-38, 44-83, 86-88 84, 85 39-43 84, 85
1053	No abnormalities detected Hair sparse, Forefoot/left Hair sparse, Forefoot/right Hair sparse, Forelimb/left Hair sparse, Forelimb/right
	1-20 21-28 21-28 29-64 29-64
1054	No abnormalities detected Piloerection Posture hunched
	1-88, 90-96 89 97, 98

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Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>0 mg/kg/day</u>	
1054 Unkempt appearance	97, 98
1055 No abnormalities detected	1-41, 69-72
Activity decreased	86
Carriage high	86
Material around mouth, Red	85, 86
Material around nose, Red	85, 86
Swelling, Axillary region/left	73-86
Swelling, Thoracic region	42-68
Thin	86
Unkempt appearance	86
1056 No abnormalities detected	1-9, 13-57
Hair sparse, Cervical region	10-12
1057 No abnormalities detected	1-79, 82, 83
Carriage low	84-89
Feces watery	80, 81
Material around nose, Brown	84-89
Material around nose, Red	90-96
1058 No abnormalities detected	1-67, 72-81
Swelling, Axillary region/right	68-71
1059 No abnormalities detected	1-24

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Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>0 mg/kg/day</u>	
1059 Hair sparse, Ventral surface	25-27
1060 No abnormalities detected	1-11
Hair sparse, Abdominal region	12-25
Hair sparse, Cervical region	16-28
Hair sparse, Forefoot/right	31-88
Hair sparse, Forelimb/left	19-90, 95-99
Hair sparse, Shoulder/right	25-30
Hair sparse, Thoracic region	12-30
Piloerection	89, 92-99
Skin warm to touch, Entire body	25-37
Unkempt appearance	84-99
1061 No abnormalities detected	1-5, 13-71
Hair sparse, Cervical region	6-12
1062 No abnormalities detected	1-28, 30-88, 91-94
Feces soft	29, 89
Nodule, 1-5 mm, Dorsal surface	95-103
Scabbed area, Hind foot/left	89, 90
Teeth broken	95
Unkempt appearance	97
1063 ^{1,r} No abnormalities detected	3-88

¹ No observation for Week(s) 1-2

^r Replacement animal

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number		Week(s) Sign Present
<u>0 mg/kg/day</u>		
1063 ^{1,r}	Piloerection	92-98
	Scabbed area, Hind foot/left	89-98
	Swelling, Hind foot/right	92-98
	Ulcer plantar/palmar, >20 mm, Hind foot/right	89-98
	Unkempt appearance	92-98
1064	No abnormalities detected	1-71
1065	No abnormalities detected	1-82
1066	No abnormalities detected	1-62
	Hair sparse, Nose/muzzle	63-67
1067	No abnormalities detected	1-4, 22-86
	Eye discolored, Pale, Eye/left	97-103
	Eye discolored, White, Eye/right	96-103
	Hair discolored, Brown, Ventral surface	89-103
	Hair discolored, Yellow, Abdominal region	87, 88
	Hair sparse, Forefoot/left	5-21
	Hair sparse, Forefoot/right	5-11
1068	No abnormalities detected	1-5, 29-45, 70-83
	Hair discolored, Brown, Face	97-103
	Hair discolored, Tan, Face	84-89

¹ No observation for Week(s) 1-2

^r Replacement animal

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>0 mg/kg/day</u>	
1068	Hair discolored, Yellow, Ventral surface 84-103
	Hair sparse, Face 46-69
	Hair sparse, Forefoot/left 6-28
	Hair sparse, Forefoot/right 6-28
	Swelling, Axillary region/right 102, 103
1069	No abnormalities detected 1
	Feces soft 69
	Hair sparse, Forefoot/left 7-28
	Hair sparse, Forefoot/right 7-28
	Lacrimation, Eye/right 39-55
	Malocclusion 25-77
	Material around eyes, Black, Eye/right 26-38, 56-77
	Material around eyes, Red, Eye/right 15-17, 25, 39-55
	Nodule, 1-5 mm, Elbow/left 51-77
	Swelling, Face 55, 59-77
	Swelling, Upper jaw 38-55
	Teeth cut 36-39, 54, 55, 57, 58, 65-77
	Teeth missing 2-77
	Vocalization 55-77
1070	No abnormalities detected 1-5, 29, 30, 38-74
	Activity decreased 75
	Hair sparse, Forefoot/right 6-28

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Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>0 mg/kg/day</u>	
1070	Hair sparse, Thoracic region 31-37
	Head tilt 75
	Material around eyes, Red, Eye/left 7-9
	Righting reflex impaired 75
1071	No abnormalities detected 1-88
	Hair discolored, Brown, Anogenital region 89-101
	Hair discolored, Brown, Ventral surface 97-101
	Hair wet, Abdominal region 97-101
	Swelling, Axillary region/left 96-101
	Swelling, Hind foot/right 101
1072	No abnormalities detected 1-42, 52-68, 70-96
	Hair discolored, Brown, Ventral surface 97, 98
	Material around eyes, Red, Eye/left 43-51, 69
1073	No abnormalities detected 1
	Hair sparse, Dorsal surface 95
	Hair sparse, Forefoot/left 2-21
	Hair sparse, Forefoot/right 5-88
	Nodule, 1-5 mm, Face 95
	Swelling, Inguinal region/right 83-95
1074	No abnormalities detected 1-4, 7-54

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>0 mg/kg/day</u>	
1074	Activity decreased 55
	Carriage low 55
	Scabbed area, Face 5, 6
1075	No abnormalities detected 1-101
	Posture hunched 102, 103
1076	No abnormalities detected 1-96
	Swelling, Axillary region/right 97-103
1077	No abnormalities detected 1-38, 89-93
	Abrasion(s), Nose/muzzle 96
	Hair discolored, Brown, Ventral surface 97-103
	Hair sparse, Dorsal surface 97-103
	Hair sparse, Thoracic region 39-88
	Material around eyes, Black, Eye/left 88
	Nodule, 1-5 mm, Thoracic region 97-103
	Piloerection 103
	Posture hunched 94-103
	Thin 99-103
	Unkempt appearance 97-103
1078	No abnormalities detected 1-81, 84-87
	Discharge, Red, Penis 82, 83

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>0 mg/kg/day</u>	
1079	No abnormalities detected 1-83
	Carriage low 86-88
	Hair discolored, Yellow, Ventral surface 84-88
1080	No abnormalities detected 1-79, 89-98
	Material around nose, Brown 80-88
<u>0.1 mg/kg/day</u>	
1081	No abnormalities detected 1-52
1082	No abnormalities detected 1-48, 50-52
	Material around eyes, Red, Eye/left 49
1083	No abnormalities detected 1-39, 41-48
	Nodule, 1-5 mm, Lip 49-52
	Scabbed area, Digit 40
1084	No abnormalities detected 1-52
1085	No abnormalities detected 1-52
1086	No abnormalities detected 1-52

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>0.1 mg/kg/day</u>	
1087	No abnormalities detected 1-52
1088	No abnormalities detected 1-5, 38, 40-52 Hair sparse, Face 29-37 Hair sparse, Forefoot/left 6-20, 25 Hair sparse, Forefoot/right 6-25 Malocclusion 39 Scabbed area, Face 26-37 Teeth broken 39
1089	No abnormalities detected 1-24 Hair sparse, Shoulder/left 25-52 Hair sparse, Shoulder/right 25-52
1090	No abnormalities detected 1-15, 25-52 Hair sparse, Forefoot/left 16-24 Hair sparse, Forefoot/right 19-24
1091	No abnormalities detected 1-23, 54-56, 64-78, 80, 81 Hair sparse, Abdominal region 29-53 Hair sparse, Ventral surface 24-28 Nodule, 1-5 mm, Anogenital region 89-103 Nodule, 1-5 mm, Dorsal surface 82, 83

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>0.1 mg/kg/day</u>	
1091	Nodule, 1-5 mm, Thoracic region Nodule, 5-20 mm, Dorsal surface Nodule, 5-20 mm, Thoracic region Scabbed area, Dorsal surface Scabbed area, Thoracic region Vocalization
	32-35, 57-63 84-103 36-53 84-103 50-53 79, 102
1092	No abnormalities detected
	1-58
1093	No abnormalities detected Hair sparse, Thoracic region Scabbed area, Thoracic region
	1-26, 52-56, 61-103 27-51 27-51, 57-60
1094	No abnormalities detected Scabbed area, Thoracic region
	1-25, 27-103 26
1095	No abnormalities detected Nodule, 1-5 mm, Face Scabbed area, Cervical region Scabbed area, Face
	1-23, 31-35 36-72 24-27 28-30
1096	No abnormalities detected Hair discolored, Brown, Dorsal surface Piloerection
	1-38, 41-79 89-103 89

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Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number		Week(s) Sign Present
<u>0.1 mg/kg/day</u>		
1096	Posture hunched	102, 103
	Scabbed area, Dorsal surface	80-88
	Swelling, Inguinal region/left	96-103
	Swelling, Inguinal region/right	96-103
	Unkempt appearance	89-103
	Vocalization	39, 40, 101, 102
1097	No abnormalities detected	1-74, 80-88
	Hair discolored, Yellow, Anogenital region	89-103
	Hair wet, Anogenital region	99-103
	Nodule, 1-5 mm, Lumbar region	97-103
	Swelling, Hind limb/left	75-79
	Swelling, Hind limb/right	75-79
	Teeth cut	89-94, 98-103
	Ulcer plantar/palmar, 1-5 mm, Hind foot/left	99-103
	Ulcer plantar/palmar, 1-5 mm, Hind foot/right	99-103
	Unkempt appearance	97-103
1098	No abnormalities detected	1-79, 82-90
	Material around nose, Red	80, 81
	Unkempt appearance	91
1099	No abnormalities detected	1-37, 64-94, 99
	Abrasion(s), Anogenital region	103

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Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>0.1 mg/kg/day</u>	
1099	Hair sparse, Shoulder/left Hair sparse, Shoulder/right Material around eyes, Brown, Eye/right Material around eyes, Red, Eye/right Scabbed area, Anogenital region Swelling, Anogenital region
	38-55 38-63 95-98 100-103 102, 103 101-103
1100	No abnormalities detected
	1-94
1101	No abnormalities detected Hair sparse, Forefoot/left Hair sparse, Forefoot/right
	1-15, 22-24, 39-55 16-21, 25-38 25-38
1102	No abnormalities detected Nodule, 1-5 mm, Dorsal surface Scabbed area, Dorsal surface
	1-79 89-92 80-92
1103	No abnormalities detected
	1-19
1104	No abnormalities detected
	1-62
1105	No abnormalities detected Activity decreased Eyelid partially/completely closed, Eye/left
	1-28, 30-65 93 93

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>0.1 mg/kg/day</u>	
1105	Eyelid partially/completely closed, Eye/right 93
	Feces few/absent 93
	Feces soft 29
	Hair sparse, Forefoot/right 66-88
	Hair sparse, Forelimb/right 79-93
	Hair sparse, Periocular/right 89-93
	Inappetence 93
	Lacrimation, Eye/right 88-93
	Posture hunched 93
	Scabbed area, Face 87-93
1106	No abnormalities detected 1-41
1107	No abnormalities detected 1-97
	Piloerection 103
	Skin discolored, Brown, Tail 98-103
	Unkempt appearance 98-102
1108	No abnormalities detected 1-64, 70-80
	Limb function impaired, Hind limb/right 89
	Swelling, Axillary region/left 65-69
	Swelling, Hind foot/right 81-89
1109	No abnormalities detected 1-27, 31-103

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>0.1 mg/kg/day</u>	
1109	Material around eyes, Red, Eye/right 28-30
1110	No abnormalities detected 1-57, 59-78
	Carriage low 98
	Discharge, Red, Vulva 58
	Hair sparse, Abdominal region 83-88
	Hair sparse, Anogenital region 90-98
	Hair wet, Ventral surface 97, 98
	Swelling, Anogenital region 79-95
1111	No abnormalities detected 1, 3-5
	Breathing audible 46
	Breathing difficult 46
	Eye discolored, Dark, Eye/left 46
	Hair sparse, Face 2, 6-46
	Material around mouth, Red 46
	Vocalization 46
1112	No abnormalities detected 1-82
	Hair discolored, Brown, Dorsal surface 103
	Nodule, 1-5 mm, Nose/muzzle 89-103
	Nodule, 1-5 mm, Thoracic region 97-103
	Piloerection 103
	Swelling, Inguinal region/left 92-103

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Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>0.1 mg/kg/day</u>	
1112 Swelling, Inguinal region/right	83-103
Vocalization	102, 103
1113 No abnormalities detected	1-6
Hair sparse, Dorsal surface	89
Hair sparse, Forefoot/left	7-55
Hair sparse, Forefoot/right	10-88
Hair sparse, Forelimb/left	89
Hair sparse, Forelimb/right	61-88
Hair sparse, Shoulder/right	89
Scabbed area, Dorsal surface	89
Scabbed area, Ear/right	67-73
Teeth cut	79-83
Vocalization	38, 84-88
1114 No abnormalities detected	1-6, 31-71
Hair sparse, Face	12-30
Scabbed area, Face	7-13
Swelling, Hind foot/left	72
Swelling, Hind foot/right	72
1115 No abnormalities detected	1-56
Nodule, 1-5 mm, Lumbar region	57-75
Nodule, 5-20 mm, Lumbar region	76-92

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>0.1 mg/kg/day</u>	
1115	Scabbed area, Lumbar region 89-92
	Swelling, Axillary region/left 83-85
	Swelling, Cervical region 80-85
	Vocalization 64, 65
1116	No abnormalities detected 1-3
1117	No abnormalities detected 1-69
	Eye discolored, White, Eye/left 83-89
	Eye discolored, White, Eye/right 83-89
	Hair discolored, Brown, Ventral surface 70-89
	Unkempt appearance 84-88
1118	No abnormalities detected 1-25
	Hair discolored, Brown, Ventral surface 84
	Hair sparse, Cervical region 26-55
	Hair sparse, Thoracic region 32-55
	Nodule, 1-5 mm, Dorsal surface 49-84
	Unkempt appearance 74-84
1119	No abnormalities detected 1-50
1120	No abnormalities detected 1-88, 90-103
	Swelling, Inguinal region/left 89

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number		Week(s) Sign Present
<u>0.1 mg/kg/day</u>		
1120	Swelling, Inguinal region/right	89
1121	No abnormalities detected	1-83
	Activity decreased	84
	Eyelid partially/completely closed, Eye/left	84
	Eyelid partially/completely closed, Eye/right	84
1122	No abnormalities detected	1-65, 89-91
	Eye protruding, Eye/left	92-102
	Eye protruding, Eye/right	97-102
	Nodule, 1-5 mm, Axillary region/left	66-88
	Nodule, 1-5 mm, Shoulder/left	98-103
1123	No abnormalities detected	1-82
	Hair sparse, Abdominal region	97-103
	Hair sparse, Thoracic region	89-96
	Hair wet, Abdominal region	97-103
	Nodule, 1-5 mm, Thoracic region	83
	Nodule, 5-20 mm, Thoracic region	84-103
	Unkempt appearance	103
1124	No abnormalities detected	1-100
	Hair discolored, Yellow, Anogenital region	101-103
1125	No abnormalities detected	1-5, 31-95

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>0.1 mg/kg/day</u>	
1125	Activity decreased 100
	Hair sparse, Abdominal region 97-100
	Hair sparse, Forefoot/left 6-30
	Hair sparse, Forefoot/right 10-17
	Hair sparse, Forelimb/left 18-24
	Hair wet, Abdominal region 97-100
	Material around eyes, Black, Eye/left 100
	Swelling, Inguinal region/left 96-100
	Swelling, Inguinal region/right 96-100
1126	No abnormalities detected 1-97
	Activity decreased 98
1127	No abnormalities detected 1-13, 32-49, 52-82
	Hair discolored, Brown, Dorsal surface 89-103
	Hair sparse, Dorsal surface 89-103
	Hair sparse, Face 14-31, 50, 51
	Nodule, 1-5 mm, Thoracic region 89-95
	Nodule, 5-20 mm, Dorsal surface 102, 103
	Piloerection 89
	Scabbed area, Face 14, 15, 50, 51
	Scabbed area, Thoracic region 89-95
	Swelling, Axillary region/left 83-88
	Unkempt appearance 89-103

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>0.1 mg/kg/day</u>	
1128	No abnormalities detected 1-74
	Activity decreased 79
	Righting reflex lost 79
	Swelling, Cranial region 75-79
	Unkempt appearance 79
1129	No abnormalities detected 1-22, 25-81
	Material around nose, Black 23, 24
	Material around nose, Red 82-85
1130	No abnormalities detected 1-81
	Carriage low 101
	Nodule, 1-5 mm, Dorsal surface 82-101
	Scabbed area, Dorsal surface 89-101
1131	No abnormalities detected 1-64
1132	No abnormalities detected 1-103
1133	No abnormalities detected 1-90
1134	No abnormalities detected 1-97
	Nodule, 1-5 mm, Forefoot/left 99-101

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>0.1 mg/kg/day</u>	
1134 Nodule, 1-5 mm, Lumbar region	98-101
1135 No abnormalities detected	1-11
Hair sparse, Face	25-28, 67-88
Hair sparse, Forefoot/left	12-88
Hair sparse, Forefoot/right	12-88
Hair sparse, Forelimb/left	61-94
Nodule, 1-5 mm, Thoracic region	89-94
1136 No abnormalities detected	1-88
Eyelid partially/completely closed, Eye/left	91, 92
Eyelid partially/completely closed, Eye/right	91, 92
Hair discolored, Brown, Ventral surface	89-92
Posture hunched	91, 92
Thin	91, 92
Unkempt appearance	91, 92
1137 No abnormalities detected	1-35, 61-76
Nodule, 1-5 mm, Lip	36-60
1138 No abnormalities detected	1-82
Eye discolored, Cloudy, Eye/left	84-99
Eye discolored, Cloudy, Eye/right	84-99
Limb function impaired, Forelimb/left	99

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>0.1 mg/kg/day</u>	
1138	Material around nose, Brown 97-99
	Posture hunched 97-99
	Swelling, Cervical region 83-87
	Unkempt appearance 97-99
1139	No abnormalities detected 1-12
1140	No abnormalities detected 1-101, 103
	Posture hunched 102
1141	No abnormalities detected 1-4
	Hair sparse, Face 5-15
	Hair sparse, Forefoot/left 11-58
	Hair sparse, Forefoot/right 11-58
	Hair sparse, Forelimb/left 16-58
	Hair sparse, Forelimb/right 16-58
1142	No abnormalities detected 1-12, 29-55
	Hair sparse, Forefoot/left 13-28
	Hair sparse, Forefoot/right 13-28
1143	No abnormalities detected 1-88, 97-100
	Hair discolored, Brown, Dorsal surface 89-96
	Piloerection 89, 102, 103

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>0.1 mg/kg/day</u>	
1143 Posture hunched	101-103
Thin	101-103
1144 No abnormalities detected	1-11
Hair sparse, Shoulder/right	25-47
Hair sparse, Thoracic region	12-28
1145 No abnormalities detected	1-11, 29-46
Hair sparse, Face	12-28
Swelling, Hind foot/left	47
1146 No abnormalities detected	1-75
1147 No abnormalities detected	1-103
1148 No abnormalities detected	1-79
Swelling, Digit	80, 81
1149 No abnormalities detected	1-71, 80-88
Swelling, Axillary region/right	72-79
1150 No abnormalities detected	1-101
Vocalization	102, 103
1151 No abnormalities detected	1-20

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number		Week(s) Sign Present
<u>0.1 mg/kg/day</u>		
1151	Hair sparse, Forefoot/left	23-83
	Hair sparse, Forefoot/right	23-60
	Hair sparse, Forelimb/left	21-83
1152	No abnormalities detected	1-73
1153	No abnormalities detected	1-15, 18-88
	Eye discolored, Cloudy, Eye/left	89
	Eye discolored, Cloudy, Eye/right	89
	Hair sparse, Face	16, 17
	Limb function impaired, Hind limb/left	89
	Swelling, Hind foot/left	89
1154	No abnormalities detected	1-97
	Hair discolored, Yellow, Ventral surface	98-102
	Hair sparse, Anogenital region	103
	Hair sparse, Dorsal surface	103
	Unkempt appearance	98-102
1155	No abnormalities detected	1-18
	Nodule, 1-5 mm, Lumbar region	22-24
	Nodule, 5-20 mm, Lumbar region	25-31
	Nodule, >20 mm, Lumbar region	32-35
	Scabbed area, Lumbar region	19-21, 27-35

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>0.1 mg/kg/day</u>	
1156	No abnormalities detected Swelling, Cervical region Vocalization
	1-37, 40-64, 80, 81 65-79 38, 39
1157	No abnormalities detected Scabbed area, Nose/muzzle
	1-47, 49-101 48
1158	No abnormalities detected Scabbed area, Tail Ulcer, >20 mm, Tail
	1-79 80-89 89
1159	No abnormalities detected Material around nose, Brown Posture hunched
	1-96 97-101 101
1160	No abnormalities detected Swelling, Axillary region/right
	1-91 92
<u>1 mg/kg/day</u>	
1161	No abnormalities detected Hair sparse, Cervical region
	1-37 38-52
1162	No abnormalities detected
	1-30

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>1 mg/kg/day</u>	
1162	Hair sparse, Forefoot/left Hair sparse, Forefoot/right Hair sparse, Forelimb/left Hair sparse, Forelimb/right
	31-52 31-52 37-52 37-52
1163	No abnormalities detected Abrasion(s), Face
	1-44, 47-52 45, 46
1164	No abnormalities detected Hair sparse, Face
	3-14, 25-52 1, 2, 15-24
1165	No abnormalities detected Hair sparse, Forefoot/left Hair sparse, Forefoot/right Hair sparse, Forelimb/left
	1, 2, 15-26, 39 3-14, 27-38 3-14, 27-35 40-52
1166	No abnormalities detected
	1-52
1167	No abnormalities detected
	1-52
1168	No abnormalities detected
	1-52
1169	No abnormalities detected Hair sparse, Face
	1-14, 16-52 15

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>1 mg/kg/day</u>	
1170 No abnormalities detected	1-52
1171 No abnormalities detected	1-103
1172 No abnormalities detected	1-81
1173 No abnormalities detected	1-27, 36-75
Activity decreased	79
Breathing rapid	78, 79
Carriage low	78, 79
Eye discolored, Pale, Eye/right	79
Hair discolored, Brown, Dorsal surface	78, 79
Hair discolored, Yellow, Anogenital region	79
Hair sparse, Anogenital region	28-35
Material around nose, Red	79
Thin	76-79
Unkempt appearance	76-79
1174 No abnormalities detected	1-43
1175 No abnormalities detected	1-90
1176 No abnormalities detected	1-92, 97-99

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>1 mg/kg/day</u>	
1176	Nodule, 1-5 mm, Abdominal region Scabbed area, Abdominal region
	100-103 93-96
1177	No abnormalities detected Abrasion(s), Thoracic region Hair sparse, Dorsal surface Hair sparse, Face Hair sparse, Thoracic region Scabbed area, Dorsal surface Scabbed area, Face
	1, 2, 16-43 3, 4 8-12 8-15 3-15 5 5, 8, 9
1178	No abnormalities detected Hair discolored, Yellow, Anogenital region Hair discolored, Yellow, Ventral surface Hair sparse, Anogenital region Material around mouth, Red Nodule, 1-5 mm, Face Posture hunched Salivation Swelling, Inguinal region/right Unkempt appearance
	1-71 96-103 103 72-95 87-94 90-94, 100-103 97 87, 88 98, 99 77
1179	No abnormalities detected Hair sparse, Forefoot/left
	1 2-73

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>1 mg/kg/day</u>	
1179	Hair sparse, Forefoot/right 2-73 Hair sparse, Forelimb/left 8-13
1180	No abnormalities detected 1-7, 13-95 Hair discolored, Yellow, Anogenital region 96-103 Hair sparse, Face 8-12 Hair wet, Anogenital region 96, 103 Scabbed area, Face 8, 9 Ulcer plantar/palmar, 1-5 mm, Hind foot/left 98-103 Unkempt appearance 97-103
1181	No abnormalities detected 1-57
1182	No abnormalities detected 1-3, 43-64 Hair sparse, Cervical region 11-42 Hair sparse, Forefoot/left 4-25 Hair sparse, Forefoot/right 14-25 Hair sparse, Forelimb/left 8-36 Hair sparse, Forelimb/right 5-36
1183	No abnormalities detected 1-14, 25-60, 63-67 Hair sparse, Face 15-24 Limb function impaired, Hind limb/right 61, 62 Nodule, 5-20 mm, Axillary region/right 68-76

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>1 mg/kg/day</u>	
1183	Scabbed area, Axillary region/right Skin discolored, Red, Hind foot/right Swelling, Hind foot/right 68-74 61, 62 61, 62
1184	No abnormalities detected Ear/portion of ear missing, Ear/left Feces watery Hair discolored, Red, Cranial region Hair sparse, Cranial region Hair sparse, Thoracic region Hair sparse, Ventral surface Inappetence Nodule, 5-20 mm, Axillary region/left Scabbed area, Ear/left Scabbed area, Face Scabbed area, Ventral surface Swelling, Axillary region/left Unkempt appearance 1-10, 25 27-84 84 82-84 75-84 14-24 11-13 84 73-84 26 57, 58 11-13 78-84 84
1185	No abnormalities detected Hair sparse, Forefoot/left Hair sparse, Forefoot/right 1, 15-78 2-13 2-14
1186	No abnormalities detected 15-47, 50-53, 57, 58, 98

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>1 mg/kg/day</u>	
1186	Hair sparse, Forefoot/left Hair sparse, Forefoot/right Malocclusion Teeth cut
	1-14 1-14 59-97 48, 49, 54-56, 59-61, 63-76, 81, 84, 86-91, 94, 96, 99-103
1187	No abnormalities detected
	1-78
1188	No abnormalities detected Hair sparse, Forefoot/right Hair sparse, Forelimb/right Swelling, Dorsal surface Teeth broken Teeth cut
	1-12, 44-69, 73-76, 80-86 13-39 38-42 77-79 43 70-72
1189	No abnormalities detected Hair sparse, Forefoot/left Hair sparse, Forefoot/right
	1-46, 60-65 47-59 47-59
1190	No abnormalities detected Scabbed area, Forelimb/right
	1-12, 14-35 13
1191	No abnormalities detected
	1-51
1192	No abnormalities detected
	1-4, 10-12, 14-96

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number		Week(s) Sign Present
<u>1 mg/kg/day</u>		
1192	Material around eyes, Red, Eye/left	5-9, 13
	Unkempt appearance	97-103
1193	No abnormalities detected	1-73
	Hair discolored, Brown, Dorsal surface	103
	Hair discolored, Yellow, Ventral surface	103
	Nodule, 1-5 mm, Thoracic region	74-103
	Swelling, Axillary region/right	96
	Swelling, Hind foot/left	98-102
	Unkempt appearance	103
1194	No abnormalities detected	1-85, 87-93
	Discharge, Red, Penis	86
	Hair discolored, Yellow, Ventral surface	103
	Hair sparse, Forefoot/left	97-103
	Hair sparse, Forefoot/right	97-103
	Hair wet, Anogenital region	103
	Posture hunched	94-103
	Thin	97-103
1195	No abnormalities detected	1-3, 14-19, 37-44
	Hair sparse, Forefoot/left	21-36
	Hair sparse, Forefoot/right	4-13, 21-36
	Hair sparse, Forelimb/left	45-86

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>1 mg/kg/day</u>	
1195	Hair sparse, Forelimb/right 45-86
	Hair wet, Abdominal region 86
	Hair wet, Anogenital region 86
	Limb function impaired, Hind limb/left 86
	Limb function impaired, Hind limb/right 86
	Swelling, Axillary region/left 20-34
	Unkempt appearance 86
1196	No abnormalities detected 1
	Hair sparse, Cervical region 14-93
	Hair sparse, Face 2-39
	Hair sparse, Forefoot/right 19-35
	Hair sparse, Forelimb/left 19-93
	Nodule, 5-20 mm, Face 90-93
	Salivation 88-93
	Scabbed area, Face 3-13
	Swelling, Face 86-89
1197	No abnormalities detected 1-66
1198	No abnormalities detected 1-12, 14-75
	Limb function impaired, Hind limb/right 79-81
	Material around eyes, Red, Eye/left 13, 86-89
	Material around nose, Brown 80-89

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number		Week(s) Sign Present
<u>1 mg/kg/day</u>		
1198	Swelling, Hind foot/right	76-89
1199	No abnormalities detected	1-76, 78-95, 97-103
	Hair wet, Anogenital region	96
	Material around nose, Black	77
1200	No abnormalities detected	1-57
	Lacrimation, Eye/left	69-78
	Material around eyes, Black, Eye/left	86-96
	Nodule, 1-5 mm, Thoracic region	58, 59
	Nodule, 5-20 mm, Thoracic region	60-96
1201	No abnormalities detected	1-11, 13-66, 77
	Material around eyes, Black, Eye/left	12
	Vocalization	67-76
1202	No abnormalities detected	1-3, 35-37, 77-85
	Eye discolored, Pale, Eye/left	96-102
	Hair discolored, Brown, Dorsal surface	103
	Hair sparse, Cervical region	46-57
	Hair sparse, Face	4-34
	Hair sparse, Inguinal region/left	38-57
	Hair sparse, Inguinal region/right	38-57
	Hair sparse, Shoulder/right	58-76

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number		Week(s) Sign Present
<u>1 mg/kg/day</u>		
1202	Lacrimation, Eye/left	88-100
	Lacrimation, Eye/right	88-100
	Material around nose, Red	86-103
	Scabbed area, Face	4-13
	Swelling, Face	96-103
	Swelling, Periocular/left	86-95, 100-103
	Thin	102, 103
	Unkempt appearance	103
1203	No abnormalities detected	1-4, 13-43
	Hair sparse, Forefoot/left	5-12
	Hair sparse, Forefoot/right	5-12
1204	No abnormalities detected	1-14, 25-63, 68-73
	Hair discolored, Red, Dorsal surface	103
	Hair sparse, Face	15-24
	Nodule, 1-5 mm, Dorsal surface	83-103
	Swelling, Cranial region	78-82
	Unkempt appearance	103
	Vocalization	64-67, 74-77
1205	No abnormalities detected	1-66, 68-72, 75
	Material around nose, Black	76
	Nodule, 1-5 mm, Face	73, 74

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>1 mg/kg/day</u>	
1205 Urine discolored, Red	67
1206 No abnormalities detected	1-70
Nodule, 1-5 mm, Anogenital region	71-78
1207 No abnormalities detected	1-10, 14-29
Hair sparse, Axillary region/right	11-13
1208 No abnormalities detected	1-72
1209 No abnormalities detected	1-76, 78
Hair discolored, Yellow, Anogenital region	79-88
Material around nose, Red	77
1210 No abnormalities detected	1-38, 40-89, 91, 98
Nodule, 1-5 mm, Thoracic region	92-96
Nodule, >20 mm, Thoracic region	97
Teeth broken	39
Teeth cut	39
Vocalization	90
1211 No abnormalities detected	1-81
Hair discolored, Brown, Anogenital region	82-103
Hair discolored, Brown, Dorsal surface	103

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>1 mg/kg/day</u>	
1211	Hair wet, Anogenital region 100-103
	Piloerection 84-103
	Struggling during dosing 90
	Unkempt appearance 96-103
1212	No abnormalities detected 1-75, 77, 78
	Hair discolored, Yellow, Anogenital region 79-103
	Hypersensitive to touch 76
	Material around nose, Red 76
	Vocalization 76
1213	No abnormalities detected 1-88
	Material around eyes, Red, Eye/left 89
	Thin 89
1214	No abnormalities detected 1-7, 10-24
	Material around eyes, Black, Eye/right 8, 9
	Nodule, 1-5 mm, Forefoot/left 25-68
1215	No abnormalities detected 1-70
1216	No abnormalities detected 1-7, 14-24
	Hair sparse, Face 8-13
	Hair sparse, Forefoot/left 25-56

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>1 mg/kg/day</u>	
1216	Hair sparse, Forefoot/right Hair sparse, Forelimb/left Hair sparse, Forelimb/right Scabbed area, Face 25-56 25-56 25-56 8, 9
1217	No abnormalities detected Discharge, Yellow, Penis Eye discolored, White, Eye/left Eye discolored, White, Eye/right Hair discolored, Yellow, Anogenital region Hair sparse, Forelimb/left Material around nose, Red Nodule, 1-5 mm, Ventral surface Posture hunched Scabbed area, Ventral surface Swelling, Anogenital region 1-57, 59, 61-69 58 74-97 74-97 78-100 70-100 74, 75 88-100 60 89-100 58
1218	No abnormalities detected Hair discolored, Yellow, Ventral surface Hair sparse, Anogenital region Scabbed area, Anogenital region 1-88, 97-99 103 100-103 89-96
1219	No abnormalities detected Lacrimation, Eye/left 1-67, 75-79 68-74

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>1 mg/kg/day</u>	
1219 Lacrimation, Eye/right	68, 69
1220 No abnormalities detected	1-49, 53-69, 73-77
Hair discolored, Yellow, Anogenital region	78-97
Vocalization	50-52, 70-72
1221 No abnormalities detected	1-77, 79-85, 91-95
Feces soft	78, 86-90
Feces watery	78
Hair discolored, Yellow, Ventral surface	96-103
Unkempt appearance	101-103
1222 No abnormalities detected	1-4, 8-68
Hair sparse, Dorsal surface	5-7
1223 No abnormalities detected	1, 2, 36-73, 75-90, 96-100
Hair sparse, Face	3-34
Hair sparse, Forefoot/left	6-35
Hair sparse, Forefoot/right	5-35
Material around nose, Red	74
Nodule, 1-5 mm, Thoracic region	101-103
Piloerection	101-103
Scabbed area, Face	4-13
Swelling, Thoracic region	91-95

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>1 mg/kg/day</u>	
1223 Unkempt appearance	103
1224 No abnormalities detected	1-4, 65
Hair sparse, Cervical region	25-60
Hair sparse, Face	15-24
Hair sparse, Forefoot/left	5-24
Hair sparse, Forefoot/right	5-25, 28-37
Hair sparse, Forelimb/left	8-24
Hair sparse, Forelimb/right	8-24
Material around eyes, Red, Eye/left	66, 67
Material around eyes, Red, Eye/right	66, 67
Nodule, 1-5 mm, Cranial region	62-64
Swelling, Cranial region	61-64
1225 No abnormalities detected	1-29, 46-77
Hair discolored, Brown, Dorsal surface	103
Hair sparse, Abdominal region	78-103
Hair sparse, Anus	90-95
Swelling, Anogenital region	30-45
Swelling, Thoracic region	98, 99
Unkempt appearance	101-103
1226 No abnormalities detected	1-73
Nodule, 1-5 mm, Axillary region/right	74-76

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number		Week(s) Sign Present
<u>1 mg/kg/day</u>		
1227	No abnormalities detected	1-7, 49-100
	Hair sparse, Face	8-48
	Nodule, 1-5 mm, Lumbar region	101-103
	Piloerection	101-103
1228	No abnormalities detected	1-57
1229	No abnormalities detected	1-28, 36, 37
	Activity decreased	91-94
	Hair sparse, Forefoot/left	47-59
	Hair sparse, Hind limb/left	38-59
	Hair sparse, Inguinal region/right	47-59
	Nodule, 1-5 mm, Dorsal surface	49-59
	Nodule, 5-20 mm, Dorsal surface	60-94
	Scabbed area, Hind limb/left	38, 39
	Scabbed area, Inguinal region/left	29-32
	Swelling, Digit	33-35
	Thin	94
	Vocalization	67-77, 84-91
1230	No abnormalities detected	1-36
	Limb function impaired, Hind limb/left	37
	Limb function impaired, Hind limb/right	37

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>1 mg/kg/day</u>	
1231	No abnormalities detected Hair sparse, Forefoot/left Hair sparse, Forefoot/right
	1-4, 14-27, 29-60 5-13, 28 5-13, 28
1232	No abnormalities detected
	1-81
1233	No abnormalities detected Hair sparse, Forefoot/left Hair sparse, Forefoot/right Hair sparse, Forelimb/right
	1-7, 29-32 8-13, 26-28, 33-59 8-25 13-24
1234	No abnormalities detected
	1-58
1235	No abnormalities detected Nodule, 1-5 mm, Lumbar region Nodule, 5-20 mm, Lumbar region
	1-32, 46, 64 33-45, 47-60 61-63
1236	No abnormalities detected Hair sparse, Anogenital region Hair sparse, Dorsal surface Nodule, 1-5 mm, Cervical region Thin
	1-42, 46-89 90-102 98-102 43-45 102
1237	No abnormalities detected
	1-47

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>1 mg/kg/day</u>	
1237	Hair discolored, Brown, Anogenital region
	Limb function impaired, Hind limb/left
	Limb function impaired, Hind limb/right
	Thin
	Unkempt appearance
1238	No abnormalities detected
	Hair sparse, Forefoot/left
	Hair sparse, Forefoot/right
	Hair sparse, Forelimb/left
1239	No abnormalities detected
	Hair sparse, Cranial region
	Hair sparse, Face
	Hair sparse, Forefoot/left
	Hair sparse, Forefoot/right
	Scabbed area, Face
1240	No abnormalities detected
	Hair absent, Axillary region/left
	Hair absent, Axillary region/right
	Hair absent, Forelimb/right
	Hair sparse, Anogenital region
	Hair sparse, Cervical region

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>1 mg/kg/day</u>	
1240	Hair sparse, Forefoot/left 4-36
	Hair sparse, Forefoot/right 4-36
	Hair sparse, Forelimb/left 37
	Hair sparse, Forelimb/right 13, 37
	Hair sparse, Hind limb/right 47-103
	Hair sparse, Shoulder/left 26-64
	Hair sparse, Shoulder/right 14-25, 38-64
	Struggling during dosing 90
	Swelling, Hind foot/right 98-103
	Unkempt appearance 103
<u>50 mg/kg/day</u>	
1241	No abnormalities detected 1-52
1242	No abnormalities detected 1-52
1243	No abnormalities detected 1-36
	Hair sparse, Forefoot/left 37-52
	Hair sparse, Forefoot/right 37-52
1244	No abnormalities detected 1-19, 21-37
	Hair sparse, Forefoot/left 38-52
	Hair sparse, Forefoot/right 38-52

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>50 mg/kg/day</u>	
1244 Material around eyes, Red, Eye/left	20
1245 No abnormalities detected	1-32, 52
Hair sparse, Abdominal region	35-51
Scabbed area, Abdominal region	33-37
1246 No abnormalities detected	1-52
1247 No abnormalities detected	1-52
1248 No abnormalities detected	1-4, 8-52
Hair sparse, Forefoot/left	5-7
1249 ^r No abnormalities detected	1-10, 29-52
Abrasion(s), Face	12, 13
Hair sparse, Face	11-28
Scabbed area, Face	14-27
1250 No abnormalities detected	1-4, 6, 7, 16-52
Hair sparse, Face	5, 8-15
Scabbed area, Face	5, 8, 9
1251 No abnormalities detected	1-87, 96-103
Hypersensitive to touch	88-95

^r Replacement animal

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>50 mg/kg/day</u>	
1251 Vocalization	88-95
1252 No abnormalities detected	1-84, 95
Hair wet, Anogenital region	96-98
Vocalization	85-94, 96-103
1253 No abnormalities detected	1-84
Posture hunched	85-87
1254 No abnormalities detected	1-62, 71-73, 77-103
Vocalization	63-70, 74-76
1255 No abnormalities detected	1-100
Unkempt appearance	101-103
1256 No abnormalities detected	1-65
1257 No abnormalities detected	1-66
Hair discolored, Brown, Anogenital region	103
Nodule, 1-5 mm, Dorsal surface	67-103
Scabbed area, Dorsal surface	67-103
1258 No abnormalities detected	1-87
Hypersensitive to touch	88-96

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>50 mg/kg/day</u>	
1258 Vocalization	88-96
1259 No abnormalities detected	1-65
1260 No abnormalities detected	1-98
Hypersensitive to touch	99-102
Limb function impaired, Hind limb/left	99-102
Limb function impaired, Hind limb/right	99-102
Vocalization	99-102
1261 No abnormalities detected	1-103
1262 No abnormalities detected	1-4, 37-82
Malocclusion	5-23
Swelling, Digit	24-36
Teeth broken	5-15
1263 No abnormalities detected	1-86
1264 No abnormalities detected	1-33
Hair discolored, Yellow, Ventral surface	77-79
Hair sparse, Anogenital region	34-79
Material around eyes, Black, Eye/left	79
Nodule, 1-5 mm, Forefoot/right	56-79

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>50 mg/kg/day</u>	
1264 Scabbed area, Forefoot/left	79
1265 No abnormalities detected	1-11
Swelling, Axillary region/right	63-72
Tail bent	12-72
1266 No abnormalities detected	1-83
1267 No abnormalities detected	1-76
Limb function impaired, Hind limb/left	84-89
Limb function impaired, Hind limb/right	86-89
Material around nose, Red	88, 89
Nodule, 1-5 mm, Axillary region/right	77-89
Swelling, Forefoot/left	88, 89
Swelling, Hind foot/right	86-89
Swelling, Hind limb/left	84-89
1268 No abnormalities detected	1-56
1269 No abnormalities detected	1-3, 60-92
Hair sparse, Forefoot/left	4-59
Hair sparse, Forefoot/right	4-59
1270 No abnormalities detected	1, 29-87, 95-100

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>50 mg/kg/day</u>	
1270	Hair sparse, Forefoot/left Hair sparse, Forefoot/right Hair sparse, Forelimb/right Piloerection Swelling, Axillary region/right
	2-28 2-14 5-14 101-103 88-94
1271	No abnormalities detected Hypersensitive to touch Unkempt appearance Vocalization
	1-87, 90-99 88, 89 101-103 88, 89, 100-103
1272	No abnormalities detected Breathing audible Lacrimation, Eye/left Material around eyes, Black, Eye/left Material around eyes, Red, Eye/left
	1-12, 25-29, 32, 33, 35-38, 40-48 49 13-24 17-24, 30, 31, 34, 39 13-16
1273	No abnormalities detected Breathing audible Salivation
	1-48 49-54 54
1274	No abnormalities detected Feces few/absent Posture hunched
	1-19, 34-81 82, 83 82, 83

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>50 mg/kg/day</u>	
1274 Skin discolored, Brown, Tail Thin	20-33 82, 83
1275 No abnormalities detected	1-77
1276 No abnormalities detected Posture hunched Thin	1-28, 32-84 29-31, 85 85
1277 No abnormalities detected	1-103
1278 No abnormalities detected Hypersensitive to touch Vocalization	1-58, 61-73, 76-87 59, 60 74, 75
1279 No abnormalities detected Material around eyes, Red, Eye/right	1-39, 41-70 40
1280 No abnormalities detected Hair discolored, Red, Face Material around nose, Red Nodule, 1-5 mm, Hind foot/left Nodule, 1-5 mm, Tail Scabbed area, Cervical region	1-37, 42-60 88-103 38-41, 61-103 84-91 96-103 41

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>50 mg/kg/day</u>	
1280	Ulcer plantar/palmar, 1-5 mm, Hind foot/left 91-103 Ulcer plantar/palmar, 1-5 mm, Hind foot/right 88-103
1281	No abnormalities detected 1-59
1282	No abnormalities detected 1-71 Hair discolored, Red, Cranial region 72-87 Nodule, 1-5 mm, Thoracic region 85-95 Nodule, 1-5 mm, Ventral surface 78-95
1283	No abnormalities detected 1-86 Nodule, 5-20 mm, Sacral region 87-103 Swelling, Anogenital region 99
1284	No abnormalities detected 1-48 Hair discolored, Brown, Ventral surface 49, 50 Swelling, Hind foot/right 50
1285	No abnormalities detected 1-61
1286	No abnormalities detected 1-63, 67 Body rigid 101-103 Hair discolored, Red, Face 88-103 Material around nose, Red 68-87

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>50 mg/kg/day</u>	
1286	Swelling, Hind foot/right Unkempt appearance Vocalization
	100-103 101-103 64-66
1287	No abnormalities detected Abrasion(s), Anogenital region Material around nose, Red
	1-87, 92-95 96-103 88-91
1288	No abnormalities detected Abdomen distended Hair sparse, Cervical region Hair sparse, Face Nodule, 1-5 mm, Anogenital region Nodule, 5-20 mm, Anogenital region Scabbed area, Anogenital region Scabbed area, Cervical region Scabbed area, Face Unkempt appearance
	1-37, 49-57, 68-79, 82-84 80, 81 39-48 38 58, 59 60-67 87, 88 39-48 38 85-88
1289	No abnormalities detected Abrasion(s), Anogenital region Hair sparse, Dorsal surface Hair sparse, Thoracic region Nodule, 1-5 mm, Thoracic region
	1-32 96-103 33 34-87 74-103

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>50 mg/kg/day</u>	
1289 Scabbed area, Thoracic region	39, 74-94
1290 No abnormalities detected	1-3, 29-33, 39-65
Activity decreased	80, 81
Hair sparse, Cervical region	34-38
Hair sparse, Face	4-28
Nodule, 1-5 mm, Mouth	66-81
Posture hunched	80, 81
Scabbed area, Face	4-28
1291 No abnormalities detected	1-96
Skin discolored, Brown, Tail	97-102
Ulcer plantar/palmar, 1-5 mm, Hind foot/left	101, 102
Unkempt appearance	97-102
1292 No abnormalities detected	1-63
1293 No abnormalities detected	1-7, 11, 12, 15-83
Abrasion(s), Lip	8-10
Hair sparse, Anogenital region	13, 14
Swelling, Hind foot/left	84-88
Swelling, Inguinal region/left	87, 88
1294 No abnormalities detected	1-99

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>50 mg/kg/day</u>	
1294	Abrasion(s), Thoracic region Piloerection 100 101-103
1295	No abnormalities detected Hypersensitive to touch Unkempt appearance Vocalization 1-60, 67-84, 92-100 61-66 101-103 85-91
1296	No abnormalities detected 1-58
1297	No abnormalities detected Carriage low Eye discolored, Clear, Eye/left Eye discolored, Clear, Eye/right Eye protruding, Eye/left Hair discolored, Yellow, Ventral surface Thin 1-67 77, 78 78-103 78-103 90-103 75-103 68-100
1298	No abnormalities detected Activity decreased Breathing audible Breathing shallow Material around eyes, Red, Eye/right Thin 1-51, 57-62 63 63 63 52-56 63

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number		Week(s) Sign Present
<u>50 mg/kg/day</u>		
1299	No abnormalities detected	1-84
	Activity decreased	85
1300	No abnormalities detected	1-13, 29-50
	Hair sparse, Forefoot/left	14-28
	Hair sparse, Forefoot/right	14-28
	Material around eyes, Red, Eye/left	51-57
1301	No abnormalities detected	1-78, 88-90
	Swelling, Axillary region/left	79-87
1302	No abnormalities detected	1-59
1303	No abnormalities detected	1-87
1304	No abnormalities detected	1-77
1305	No abnormalities detected	1-76
	Material around nose, Red	79
	Piloerection	77, 78
	Unkempt appearance	79
1306	No abnormalities detected	1-60

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>50 mg/kg/day</u>	
1307	No abnormalities detected 1-4, 13-68
	Body rigid 72, 73
	Hair sparse, Forefoot/left 5-12
	Hair sparse, Forefoot/right 5-12
	Material around nose, Red 85-91
	Nodule, 1-5 mm, Axillary region/right 69-91
1308	No abnormalities detected 1-4, 29-40, 60-66, 71-100
	Hair sparse, Forefoot/left 5-28, 41-59
	Hair sparse, Forefoot/right 5-28, 41-59
	Hypersensitive to touch 67-70
	Piloerection 101
	Scabbed area, Thoracic region 101
	Thin 101
1309	No abnormalities detected 1-75, 77-87
	Hair discolored, Tan, Ventral surface 88-103
	Odor 76
	Unkempt appearance 88-103
1310	No abnormalities detected 1-59
	Eye discolored, Clear, Eye/left 78-81
	Eye discolored, White, Eye/left 66-76

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>50 mg/kg/day</u>	
1310	Eye discolored, White, Eye/right 66-76
	Hair discolored, Yellow, Ventral surface 60-76
	Odor 76-81
	Posture hunched 78-81
	Thin 67-76, 78-81
1311	No abnormalities detected 1-103
1312	No abnormalities detected 1-45
1313	No abnormalities detected 1-10, 16-101
	Hair sparse, Face 11-15
1314	No abnormalities detected 1-4, 14-24, 74-100
	Hair sparse, Forefoot/right 5-13
	Hair sparse, Forelimb/left 25-73
	Hair sparse, Forelimb/right 25-73
1315	No abnormalities detected 1-73
	Body rigid 96-103
	Hypersensitive to touch 76-103
	Vocalization 74-103
1316	No abnormalities detected 1-19, 27-32, 34-36, 39-58

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number		Week(s) Sign Present
<u>50 mg/kg/day</u>		
1316	Hair sparse, Inguinal region/right	38
	Nodule, 1-5 mm, Inguinal region/right	37
	Scabbed area, Hind limb/right	33
	Scabbed area, Inguinal region/right	38
	Swelling, Axillary region/right	20-26
1317	No abnormalities detected	1-55
	Discharge, Red, Nose/muzzle	56
	Eye discolored, Cloudy, Eye/left	56
	Eye protruding, Eye/left	56
1318	No abnormalities detected	1-37, 39-45
	Abrasion(s), Hind foot/right	54
	Carriage low	46-54
	Digit(s) missing, Hind foot/left	46-54
	Hair discolored, Brown, Anogenital region	54
	Limb function impaired, Hind limb/left	46-54
	Limb function impaired, Hind limb/right	46-54
	Righting reflex lost	54
	Swelling, Digit	38
1319	No abnormalities detected	1-75, 77-87
	Laceration, Anogenital region	76
	Nodule, 1-5 mm, Axillary region/left	88-103

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - MALE

Group, Animal Number		Week(s) Sign Present
<u>50 mg/kg/day</u>		
1319	Unkempt appearance	88-103
1320	No abnormalities detected	1-59
	Posture hunched	60-62
	Thin	60-62

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Unscheduled Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>0 mg/kg/day</u>	
1018 Activity decreased	94
Limb function impaired, Hind limb/left	94
Limb function impaired, Hind limb/right	94
Swelling, Hind foot/left	94
Swelling, Hind foot/right	94
1024 Swelling, Hind foot/right	93
1029 Abrasion(s), Anogenital region	104
Discharge, Red, Anogenital region	104
1032 Activity decreased	66
Breathing shallow	66
Moribund	66
1034 Breathing difficult	64
Moribund	64
Righting reflex lost	64
1035 Breathing audible	21

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Unscheduled Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>0 mg/kg/day</u>	
1035 Rales	21
Salivation	21
1037 Struggling during dosing	90
1039 Activity decreased	102
Breathing audible	102
Breathing shallow	102
Carriage low	102
Eyelid partially/completely closed, Eye/left	102
Eyelid partially/completely closed, Eye/right	102
Limb function impaired, Hind limb/left	102
Limb function impaired, Hind limb/right	102
1040 Activity decreased	95
Carriage low	95
Piloerection	95
Posture hunched	95
1047 Activity decreased	68
Ataxia	68
Breathing difficult	68
Carriage low	68

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Unscheduled Detailed Clinical Observations - MALE

Group, Animal Number		Week(s) Sign Present
<u>0 mg/kg/day</u>		
1047	Piloerection	68
	Thin	68
1051	Activity decreased	92
	Ataxia	92
	Feces few/absent	92
	Inappetence	92
	Loss of skin elasticity	92
	Piloerection	92
	Teeth chattering	92
	Unkempt appearance	92
1056	Activity decreased	58
	Hair discolored, Black, Anogenital region	58
	Hair discolored, Black, Hind limb/left	58
	Limb function lost, Hind limb/left	58
	Limb function lost, Hind limb/right	58
	Prostration	58
	Unkempt appearance	58
	Urine discolored, Red	58
1060	Hair wet, Ventral surface	100

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Unscheduled Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>0 mg/kg/day</u>	
1060	Limb function impaired, Hind limb/left
	Limb function impaired, Hind limb/right
	Unkempt appearance
1061	Limb function impaired, Hind limb/left
	Limb function impaired, Hind limb/right
	Swelling, Hind foot/left
	Swelling, Hind foot/right
1065	Activity decreased
	Carriage low
	Material around eyes, Black, Eye/left
	Material around eyes, Black, Eye/right
	Piloerection
	Righting reflex impaired
	Thin
	Unkempt appearance
1066	Activity decreased
	Breathing audible
	Carriage low
1079	Activity decreased

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Unscheduled Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>0 mg/kg/day</u>	
1079 Carriage low	89
Eyelid partially/completely closed, Eye/left	89
Eyelid partially/completely closed, Eye/right	89
Feces watery	89
Hair discolored, Brown, Anus	89
Hair discolored, Yellow, Ventral surface	89
Piloerection	89
Righting reflex impaired	89
<u>0.1 mg/kg/day</u>	
1097 Struggling during dosing	90
1104 Breathing audible	53
Material around nose, Red	53
Salivation	53
1105 Activity decreased	93
Eyelid partially/completely closed, Eye/left	93
Eyelid partially/completely closed, Eye/right	93
Feces few/absent	93
Material around eyes, Red, Eye/left	93

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Unscheduled Detailed Clinical Observations - MALE

Group, Animal Number		Week(s) Sign Present
<u>0.1 mg/kg/day</u>		
1105	Material around eyes, Red, Eye/right	93
	Posture hunched	93
1110	Discharge, Red, Penis	61, 99
	Hair discolored, Brown, Anogenital region	99
	Hair wet, Anogenital region	99
	Limb function impaired, Hind limb/left	99
	Limb function impaired, Hind limb/right	99
	Righting reflex impaired	99
	Scabbed area, Anogenital region	99
	Swelling, Anogenital region	99
	Unkempt appearance	99
1114	Limb function impaired, Hind limb/left	73
	Swelling, Hind foot/right	73
	Swelling, Hind limb/left	73
1117	Eye discolored, Cloudy, Eye/left	90
	Eye discolored, Cloudy, Eye/right	90
	Hair discolored, Brown, Ventral surface	90
	Limb function impaired, Hind limb/left	90
	Skin discolored, Red, Hind foot/left	90

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Unscheduled Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>0.1 mg/kg/day</u>	
1117 Swelling, Hind foot/left	90
1138 Teeth cut	80
1141 Breathing audible	59
Hair sparse, Forefoot/left	59
Hair sparse, Forefoot/right	59
Moribund	59
Salivation	59
1155 Nodule, >20 mm, Thoracic region	36
Scabbed area, Thoracic region	36
1157 Activity decreased	102
Ataxia	102
Breathing shallow	102
Carriage low	102
Material around nose, Red	102
Moribund	102
Righting reflex impaired	102

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Unscheduled Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>1 mg/kg/day</u>	
1163 Abrasion(s), Face	45
1164 Abrasion(s), Face	45
1184 Activity decreased	85
Ataxia	85
Carriage low	85
Feces few/absent	85
Feces watery	85
Hypersensitive to touch	85
Limb function impaired, Hind limb/left	85
Limb function impaired, Hind limb/right	85
Piloerection	85
Prostration	85
Righting reflex impaired	85
Teeth chattering	85
Unkempt appearance	85
1190 Activity decreased	36
Discharge, Red, Penis	36
Hair wet, Ventral surface	36
Limb function impaired, Hind limb/left	36
Limb function impaired, Hind limb/right	36

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Unscheduled Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>1 mg/kg/day</u>	
1190 Righting reflex impaired	36
1191 Limb function impaired, Hind limb/left	52
Limb function impaired, Hind limb/right	52
1195 Hair discolored, Red, Lumbar region	86
Righting reflex impaired	86
Urine discolored, Red	86
1196 Material around nose, Red	93
Scabbed area, Face	93
1206 Activity decreased	79
Carriage low	79
Eyelid partially/completely closed, Eye/left	79
Feces few/absent	79
Inappetence	79
Material around nose, Red	79
Posture hunched	79
1209 Activity decreased	89

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Unscheduled Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>1 mg/kg/day</u>	
1209 Breathing shallow	89
Eyelid partially/completely closed, Eye/left	89
Eyelid partially/completely closed, Eye/right	89
Material around eyes, Red, Eye/left	89
Material around eyes, Red, Eye/right	89
Piloerection	89
Righting reflex lost	89
Skin cold to touch, Entire body	89
1211 Abrasion(s), Anogenital region	98
Hair discolored, Brown, Ventral surface	98
Hair wet, Anogenital region	98
Piloerection	98
Unkempt appearance	98
1214 Nodule, 1-5 mm, Digit	17
1217 Activity decreased	101
Hair wet, Ventral surface	101
Righting reflex impaired	101
Skin cold to touch, Entire body	101
1223 Material in pan/bedding, Red	87

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Unscheduled Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>1 mg/kg/day</u>	
1226	Activity decreased 77
	Breathing difficult 77
	Carriage low 77
	Eyelid partially/completely closed, Eye/left 77
	Eyelid partially/completely closed, Eye/right 77
	Material around mouth, Tan 77
	Righting reflex lost 77
	Salivation 77
	Skin cold to touch, Entire body 77
1227	Salivation 93
1233	Activity decreased 60
	Ataxia 60
	Breathing shallow 60
	Carriage low 60
	Eyelid partially/completely closed, Eye/left 60
	Eyelid partially/completely closed, Eye/right 60
	Feces few/absent 60
	Piloerection 60
	Prostration 60
	Skin cold to touch, Entire body 60

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Unscheduled Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>1 mg/kg/day</u>	
1233 Teeth chattering	60
Tremors	60
1237 Limb function impaired, Hind limb/left	50
Piloerection	50
Teeth broken	48
Thin	48
Unkempt appearance	50
1239 Activity decreased	88
Hair wet, Anogenital region	88
Limb function impaired, Hind limb/left	88
Limb function impaired, Hind limb/right	88
<u>50 mg/kg/day</u>	
1260 Activity decreased	103
Breathing audible	103
Breathing shallow	103
Eyelid partially/completely closed, Eye/left	103
Eyelid partially/completely closed, Eye/right	103
Material around eyes, Red	103

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Unscheduled Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>50 mg/kg/day</u>	
1260	Material around eyes, Red, Eye/left 103
	Moribund 103
	Prostration 103
	Righting reflex impaired 103
	Teeth chattering 103
1262	Fracture, Digit 24
	Stereotypy, Straub tail 24
1263	Activity decreased 87
	Breathing shallow 87
	Moribund 87
	Skin cold to touch, Entire body 87
1264	Activity decreased 80
	Breathing shallow 80
	Righting reflex lost 80
1269	Activity decreased 93
	Limb function impaired, Hind limb/left 93
	Swelling, Hind limb/left 93
1272	Activity decreased 50

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Unscheduled Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>50 mg/kg/day</u>	
1272 Breathing audible	50
Breathing difficult	50
Teeth cut	50
1273 Breathing audible	55
Breathing difficult	55
Material around mouth, Red	55
1285 Activity decreased	62
Breathing shallow	62
Breathing slow	62
Material around eyes, Red, Eye/left	62
Material around eyes, Red, Eye/right	62
Prostration	62
Righting reflex impaired	62
1286 Material around nose, Red	65
Salivation	65
1299 Activity decreased	86
Carriage low	86
Eyelid partially/completely closed, Eye/left	86
Eyelid partially/completely closed, Eye/right	86

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Unscheduled Detailed Clinical Observations - MALE

Group, Animal Number	Week(s) Sign Present
<u>50 mg/kg/day</u>	
1299 Feces few/absent	86
Piloerection	86
Teeth chattering	86
1308 Scabbed area, Thoracic region	101
1310 Activity decreased	82
Carriage low	82
Discharge, Red, Penis	82
Eye discolored, Cloudy, Eye/left	82
Eye discolored, Cloudy, Eye/right	82
Hair discolored, Black, Hind limb/left	82
Odor	82
Righting reflex impaired	82
Skin cold to touch, Entire body	82
Thin	82
1313 Swelling, Hind foot/left	102
1320 Activity decreased	63
Eyelid partially/completely closed, Eye/right	63

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Unscheduled Detailed Clinical Observations - MALE

Group, Animal Number		Week(s) Sign Present
<u>50 mg/kg/day</u>		
1320	Posture hunched	63
	Righting reflex impaired	63
	Thin	63

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number	Week(s) Sign Present
<u>0 mg/kg/day</u>	
1321 No abnormalities detected	1-49
1322 No abnormalities detected	1-24, 51, 52
Hair sparse, Face	25-50
Scabbed area, Face	25-31
1323 No abnormalities detected	1-44
1324 No abnormalities detected	1-15, 32-52
Hair sparse, Face	16-31
1325 No abnormalities detected	1-52
1326 No abnormalities detected	1-52
1327 No abnormalities detected	1-52
1328 No abnormalities detected	1-24, 52
Hair sparse, Cranial region	25-51
1329 No abnormalities detected	1-7
Hair sparse, Face	8-52
Scabbed area, Face	8-31, 38-42

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number		Week(s) Sign Present
<u>0 mg/kg/day</u>		
1330	No abnormalities detected	1-15
	Hair sparse, Cervical region	18-52
	Hair sparse, Shoulder/left	18-52
	Hair sparse, Shoulder/right	16-52
	Hair sparse, Thoracic region	18-52
	Scabbed area, Thoracic region	41-52
1331	No abnormalities detected	1-52
1332	No abnormalities detected	1-5, 7-12, 32-52
	Hair sparse, Cervical region	13, 14
	Hair sparse, Face	13-31
	Scabbed area, Face	6
1333	No abnormalities detected	1-17, 24-30, 69-97
	Breathing rapid	98
	Hair sparse, Cervical region	18-23
	Hair sparse, Face	31-68
	Posture hunched	98-100
	Scabbed area, Face	19-23
	Thin	98-100
1334	No abnormalities detected	1-76, 84-86, 89-93

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number	Week(s) Sign Present
<u>0 mg/kg/day</u>	
1334	Activity decreased 94, 95
	Posture hunched 94, 95
	Swelling, Anogenital region 87, 88
	Swelling, Axillary region/left 77-83
1335	No abnormalities detected 1-35
	Hair discolored, Brown, Face 80-89
	Hair sparse, Anogenital region 89-100
	Hair sparse, Cervical region 36-88
	Posture hunched 97-100
	Swelling, Anogenital region 62-64
1336	No abnormalities detected 1-67
	Ear/portion of ear missing, Ear/left 73-93
	Hair discolored, Brown, Face 84-89
	Hair sparse, Anogenital region 89-93
	Posture hunched 93
	Swelling, Axillary region/left 68-74
	Thin 93
1337	No abnormalities detected 1-38
	Hair discolored, Tan, Ventral surface 39-54
	Posture hunched 54
	Thin 54

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number		Week(s) Sign Present
<u>0 mg/kg/day</u>		
1338	No abnormalities detected	1-72, 82, 83, 87
	Nodule, 1-5 mm, Axillary region/left	73-81
	Scabbed area, Axillary region/right	86
	Swelling, Axillary region/right	84-86
1339	No abnormalities detected	1-63, 65-76, 89-98
	Swelling, Anogenital region	64
	Swelling, Axillary region/right	77-88, 99, 100
1340	No abnormalities detected	1-50, 80, 81, 89-94
	Nodule, 1-5 mm, Lip	51-79
	Nodule, 1-5 mm, Nose/muzzle	63-68
	Posture hunched	97, 98
	Swelling, Anogenital region	82-88, 97, 98
	Swelling, Axillary region/left	95-98
	Thin	97, 98
1341	No abnormalities detected	1-31
	Scabbed area, Axillary region/right	32-35
1342	No abnormalities detected	1-43, 47-68
	Swelling, Axillary region/right	44-46
1343	No abnormalities detected	1-24

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number		Week(s) Sign Present
<u>0 mg/kg/day</u>		
1343	Activity decreased	66-72
	Hair sparse, Face	38-72
	Hair sparse, Forefoot/left	25-72
	Hair sparse, Forefoot/right	25-72
	Material around nose, Black	65-68
	Piloerection	69-72
	Posture hunched	66-72
	Thin	69-72
1344	No abnormalities detected	1-4
	Hair sparse, Cervical region	32-58
	Hair sparse, Forefoot/left	5-58
	Hair sparse, Forefoot/right	5-58
	Hair sparse, Forelimb/left	39-58
	Hair sparse, Forelimb/right	39-58
	Hair sparse, Shoulder/left	31-58
	Hair sparse, Shoulder/right	31-58
	Hair sparse, Thoracic region	25-58
1345	No abnormalities detected	1-37, 61-81
	Hair sparse, Cervical region	38-60
	Material around nose, Black	85
	Swelling, Axillary region/right	82-85
	Swelling, Inguinal region/left	83-85

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number	Week(s) Sign Present
<u>0 mg/kg/day</u>	
1346	No abnormalities detected Swelling, Thoracic region
	1-36, 38-58 37
1347	No abnormalities detected Hair discolored, Yellow, Anogenital region Hair sparse, Forefoot/right Posture hunched Teeth cut
	1-24, 26-56 59-100 25 97-100 57, 58, 83, 90, 91, 94, 99
1348	No abnormalities detected
	1-87
1349	No abnormalities detected Activity decreased Hair sparse, Face Material around nose, Black Posture hunched Swelling, Axillary region/left
	1-20, 59-63 66 21-58 66 66 64-66
1350	No abnormalities detected
	1-66
1351	No abnormalities detected Hair discolored, Yellow, Anogenital region Hair sparse, Cervical region
	1-31 69, 70 36-70

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number	Week(s) Sign Present
<u>0 mg/kg/day</u>	
1351	Hair sparse, Thoracic region 32-70
	Swelling, Axillary region/left 59, 60
	Swelling, Axillary region/right 59, 60
1352	No abnormalities detected 1-5, 89-91
	Abrasion(s), Cranial region 33-36
	Hair discolored, Yellow, Anogenital region 92-100
	Hair sparse, Cranial region 11-17, 32-88
	Hair sparse, Face 6-31
	Hair sparse, Nose/muzzle 46-88
	Nodule, 1-5 mm, Inguinal region/right 99, 100
	Nodule, 5-20 mm, Anogenital region 99, 100
	Scabbed area, Cranial region 11-14, 32-51
	Scabbed area, Face 6-10, 29-31
	Swelling, Abdominal region 97-100
1353	No abnormalities detected 1-88, 91-96
	Nodule, 1-5 mm, Axillary region/right 98-100
	Swelling, Anogenital region 89, 90
	Swelling, Axillary region/left 97-100
	Swelling, Thoracic region 89, 90
1354	No abnormalities detected 1-62, 64-90
	Discharge, Red, Vulva 63

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number	Week(s) Sign Present
<u>0 mg/kg/day</u>	
1355	No abnormalities detected 1-62, 68-100 Swelling, Inguinal region/right 63-67
1356	No abnormalities detected 1-62 Head tilt 65, 66 Swelling, Axillary region/left 63, 64 Swelling, Axillary region/right 66 Swelling, Inguinal region/left 63, 64 Swelling, Inguinal region/right 66
1357	No abnormalities detected 1-34 Hair sparse, Cervical region 35-100 Hair sparse, Cranial region 73-100 Swelling, Cervical region 97-100
1358	No abnormalities detected 1-62 Hair sparse, Anogenital region 89-100 Hair sparse, Cervical region 69-100 Hair sparse, Face 63-88 Hair sparse, Forefoot/left 89-100 Hair sparse, Forefoot/right 89-100 Hair sparse, Forelimb/left 63-100 Hair sparse, Hind limb/left 89-100

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number	Week(s) Sign Present
<u>0 mg/kg/day</u>	
1358	Hair sparse, Thoracic region 80-100
	Nodule, 1-5 mm, Axillary region/right 73-88
	Skin discolored, Black, Thoracic region 89
	Swelling, Axillary region/left 98-100
	Swelling, Axillary region/right 65-68
	Swelling, Thoracic region 89, 90
1359	No abnormalities detected 1-21, 25-38
	Activity decreased 67-72
	Carriage low 70-72
	Hair discolored, Yellow, Ventral surface 70-72
	Material around eyes, Red, Eye/left 22-24
	Material around nose, Red 67, 68
	Posture hunched 67-72
	Swelling, Anogenital region 39-62
	Swelling, Axillary region/right 44-66
	Thin 70-72
1360	No abnormalities detected 1-19, 36-73, 75-91
	Hair sparse, Face 24-30
	Hair sparse, Nose/muzzle 31-35
	Scabbed area, Face 20-23
	Swelling, Inguinal region/left 74
1361	No abnormalities detected 1-78, 83-93

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number	Week(s) Sign Present
<u>0 mg/kg/day</u>	
1361 Swelling, Inguinal region/left	79-82
1362 No abnormalities detected	1-79
Skin discolored, Blue, Anogenital region	89-91
Swelling, Axillary region/right	89-91
Swelling, Thoracic region	80-88
1363 No abnormalities detected	1-86
1364 No abnormalities detected	1-69
1365 No abnormalities detected	1-89, 92, 97
Hair discolored, Yellow, Ventral surface	98-100
Teeth cut	90, 91, 93-96, 99, 100
1366 No abnormalities detected	1-56, 67-72, 82, 88
Material around nose, Black	73-81
Skin discolored, Blue, Inguinal region/right	89-91
Swelling, Anogenital region	83-87
Swelling, Cervical region	57-66
1367 No abnormalities detected	1-88
1368 No abnormalities detected	1-61, 68-91

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number	Week(s) Sign Present
<u>0 mg/kg/day</u>	
1368	Hair sparse, Anogenital region 92-100
	Posture hunched 97-100
	Swelling, Inguinal region/right 62-67
	Thin 97-100
1369	No abnormalities detected 1-79
	Swelling, Inguinal region/left 82-87
	Swelling, Inguinal region/right 80-85
1370	No abnormalities detected 1-100
1371	No abnormalities detected 1-20
	Limb function impaired, Hind limb/left 21-28, 39-47
	Swelling, Hind foot/left 21-47
1372	No abnormalities detected 1-66, 68-88
	Hair sparse, Periocular/right 89-100
	Material around eyes, Black, Eye/right 94-100
	Skin discolored, Brown, Tail 97-100
	Swelling, Cervical region 67
1373	No abnormalities detected 1-12
	Carriage high 51
	Hair sparse, Face 13-51

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number		Week(s) Sign Present
<u>0 mg/kg/day</u>		
1373	Hair sparse, Forefoot/right	25-51
	Piloerection	51
	Posture hunched	51
	Scabbed area, Abdominal region	50, 51
	Swelling, Anogenital region	29-34
	Swelling, Axillary region/right	34, 35
1374	No abnormalities detected	1-15
	Hair discolored, Yellow, Anogenital region	60-100
	Hair sparse, Shoulder/left	18-88
	Hair sparse, Shoulder/right	16-88
	Hair sparse, Thoracic region	36-88
1375	No abnormalities detected	1-28
	Activity decreased	66
	Righting reflex impaired	66
	Swelling, Anogenital region	38-64
	Swelling, Axillary region/left	34-66
	Swelling, Axillary region/right	29-33, 37-66
	Swelling, Inguinal region/left	38-62
	Swelling, Inguinal region/right	63-66
	Thin	66
1376	No abnormalities detected	1-61, 63-81

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number	Week(s) Sign Present
<u>0 mg/kg/day</u>	
1376 Swelling, Anogenital region	62
Swelling, Axillary region/right	82-86
1377 No abnormalities detected	1-15, 18-28, 31-56
Hair discolored, Yellow, Ventral surface	16, 17
Hair sparse, Face	29, 30
1378 No abnormalities detected	1-73
Activity decreased	74
1379 No abnormalities detected	1-17
Activity decreased	65
Hair sparse, Cervical region	29-65
Hair sparse, Cranial region	33-65
Hair sparse, Face	18-65
Material around nose, Black	64, 65
Righting reflex impaired	65
1380 No abnormalities detected	1-51
1381 No abnormalities detected	1-18, 48, 49
Activity decreased	66
Hair sparse, Face	19-47, 50-66
Head tilt	66

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number	Week(s) Sign Present
<u>0 mg/kg/day</u>	
1381	Material around eyes, Black, Eye/left Material around eyes, Red, Eye/left Scabbed area, Face 47 52-66 32-37
1382	No abnormalities detected Swelling, Ear/right 1-72, 75-79 73, 74
1383	No abnormalities detected Swelling, Axillary region/right 1-53, 61-78 54-60
1384	No abnormalities detected Hair sparse, Face Hair sparse, Forefoot/right Hair sparse, Thoracic region Scabbed area, Face Skin discolored, Blue, Anogenital region Skin discolored, Blue, Axillary region/left Skin discolored, Blue, Axillary region/right Swelling, Axillary region/left Swelling, Axillary region/right Swelling, Inguinal region/right 1-12 13-88 53-88 31-88 13-52 89-91 89-91 89-91 73-83 67-83 65-69, 79-83
1385	No abnormalities detected Hair sparse, Axillary region/right 1-12, 39-43, 91 92-94

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number	Week(s) Sign Present
<u>0 mg/kg/day</u>	
1385	Hair sparse, Cervical region 13-38
	Hair sparse, Forefoot/left 57-88
	Hair sparse, Forefoot/right 44-90
	Scabbed area, Axillary region/right 92-94
1386	No abnormalities detected 1-44
	Activity decreased 88
	Hair discolored, Tan, Face 84-88
	Hair sparse, Forefoot/left 45-88
	Hair sparse, Forefoot/right 45-88
	Material around nose, Red 88
1387	No abnormalities detected 1-71
	Activity decreased 74-76
	Posture hunched 72-76
1388	No abnormalities detected 1-64
1389	No abnormalities detected 1-7
	Hair discolored, Brown, Face 89
	Hair discolored, Yellow, Anogenital region 70-100
	Hair sparse, Face 8-88
	Hair sparse, Forefoot/left 53-88
	Hair sparse, Forefoot/right 53-88

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number		Week(s) Sign Present
<u>0 mg/kg/day</u>		
1389	Scabbed area, Face	8-30
	Swelling, Inguinal region/right	94-100
1390	No abnormalities detected	1-25
	Hair sparse, Forefoot/left	26-87
	Hair sparse, Forefoot/right	26-87
	Nodule, 1-5 mm, Axillary region/right	73-83
	Reproductive tract prolapsed	87
	Swelling, Anogenital region	86
	Swelling, Axillary region/left	67-71
	Swelling, Cervical region	79-81
	Swelling, Inguinal region/left	52-62
1391	No abnormalities detected	1-4, 15-96
	Activity decreased	97
	Hair sparse, Forefoot/left	5-14
	Hair sparse, Forefoot/right	5-14
	Head tilt	97
	Piloerection	97
	Thin	97
1392	No abnormalities detected	1-38, 69-79, 89-91
	Hair discolored, Brown, Face	80-88
	Hair discolored, Yellow, Anogenital region	92-100

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number	Week(s) Sign Present
<u>0 mg/kg/day</u>	
1392	Hair sparse, Face 39-68 Swelling, Axillary region/right 97-100
1393	No abnormalities detected 1-14 Hair sparse, Forefoot/left 15-17, 19-87 Hair sparse, Forefoot/right 15-87 Malocclusion 86, 87 Nodule, 1-5 mm, Face 82-87 Swelling, Anogenital region 65-74 Teeth broken 86, 87 Teeth cut 87
1394	No abnormalities detected 1-7 Hair sparse, Face 8-96 Hair sparse, Forefoot/left 52-88 Hair sparse, Forefoot/right 52-88 Nodule, 1-5 mm, Axillary region/right 80-88 Posture hunched 94-96 Scabbed area, Face 8-20, 31, 36-53 Swelling, Cervical region 83 Thin 94-96
1395	No abnormalities detected 1-4 Hair sparse, Cervical region 5-61

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number	Week(s) Sign Present
<u>0 mg/kg/day</u>	
1395	Hair sparse, Thoracic region 13-61
	Head tilt 61
	Righting reflex impaired 61
1396	No abnormalities detected 1-66
	Activity decreased 67-69
	Carriage low 69
	Hair discolored, Red, Face 69
	Head tilt 69
	Material around nose, Red 67-69
	Piloerection 69
1397	No abnormalities detected 1-34
	Hair sparse, Cranial region 35-88
	Hair sparse, Face 35-88
	Hair sparse, Shoulder/right 89-100
	Hair sparse, Thoracic region 47-88
	Scabbed area, Shoulder/right 89-100
	Swelling, Anogenital region 99, 100
1398	No abnormalities detected 1-64, 79-88, 91
	Activity decreased 94
	Material around nose, Black 92-94
	Piloerection 92-94

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number	Week(s) Sign Present
<u>0 mg/kg/day</u>	
1398	Posture hunched 92-94
	Swelling, Anogenital region 89, 90
	Swelling, Inguinal region/left 65-78
	Thin 92-94
1399	No abnormalities detected 1-17
	Hair sparse, Cervical region 50
	Hair sparse, Face 18-50
	Limb function impaired, Hind limb/left 50
	Limb function impaired, Hind limb/right 50
	Scabbed area, Face 18-30
1400	No abnormalities detected 1-42
	Activity decreased 89
	Eyelid partially/completely closed, Eye/right 89
	Hair sparse, Cervical region 89
	Hair sparse, Forefoot/right 89
	Hair sparse, Forelimb/left 43-89
	Hair sparse, Forelimb/right 43-88
	Head tilt 89
	Material around eyes, Black, Eye/right 89
	Scabbed area, Cervical region 89
	Swelling, Abdominal region 83-86
	Swelling, Axillary region/left 80-89

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number		Week(s) Sign Present
<u>0 mg/kg/day</u>		
1400	Swelling, Cervical region	79-81
	Swelling, Inguinal region/left	79-89
	Swelling, Thoracic region	87, 88
<u>1 mg/kg/day</u>		
1401	No abnormalities detected	1-14, 16-29, 34-52
	Material around eyes, Red, Eye/right	15, 30-33
1402	No abnormalities detected	1
	Hair sparse, Abdominal region	28-52
	Hair sparse, Anogenital region	28-52
	Hair sparse, Forefoot/left	2-52
	Hair sparse, Forefoot/right	2-52
	Hair sparse, Forelimb/left	28-52
	Hair sparse, Forelimb/right	28-52
	Hair sparse, Hind limb/left	28-38
1403	No abnormalities detected	1-12
	Hair sparse, Anogenital region	28-36, 38-52
	Hair sparse, Cervical region	13-52
	Hair sparse, Forefoot/left	25-38
	Hair sparse, Forefoot/right	16-52
	Swelling, Anogenital region	38-42

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number		Week(s) Sign Present
<u>1 mg/kg/day</u>		
1404	No abnormalities detected	1-10
	Hair sparse, Forefoot/left	11-24, 27, 28
	Hair sparse, Forefoot/right	11-52
1405	No abnormalities detected	1-12, 25, 26
	Hair sparse, Cervical region	27-52
	Hair sparse, Forefoot/left	33-52
	Hair sparse, Forelimb/left	13-18
	Hair sparse, Forelimb/right	13-18
	Hair sparse, Shoulder/left	13-24
	Hair sparse, Shoulder/right	13-24
	Hair sparse, Thoracic region	18-24
	Hair sparse, Ventral surface	13, 14
	Swelling, Thoracic region	42
1406	No abnormalities detected	1-12
	Hair sparse, Anogenital region	30-52
	Hair sparse, Cervical region	36-52
	Hair sparse, Forelimb/left	13-52
	Hair sparse, Forelimb/right	13-52
	Hair sparse, Sacral region	37-52
	Scabbed area, Cervical region	39-44
1407	No abnormalities detected	1-52

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number		Week(s) Sign Present
<u>1 mg/kg/day</u>		
1408	No abnormalities detected	1-32, 38-52
	Nodule, 1-5 mm, Axillary region/left	33-37
1409	No abnormalities detected	1-28, 35-52
	Scabbed area, Face	29-34
1410	No abnormalities detected	1-52
1411	No abnormalities detected	1-17, 25-32, 43-50
	Hair sparse, Forelimb/right	51-57
	Hair sparse, Thoracic region	18-24, 33-42
1412	No abnormalities detected	1-51
	Ear/portion of ear missing, Ear/left	68-97
	Hair sparse, Anogenital region	80-97
	Hair sparse, Cranial region	52-97
	Skin discolored, Blue, Anogenital region	96, 97
	Swelling, Anogenital region	63-74
1413	No abnormalities detected	1-6
	Hair sparse, Forefoot/right	33-86
	Hair sparse, Forelimb/left	7-35
	Hair sparse, Forelimb/right	7-86

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number	Week(s) Sign Present
<u>1 mg/kg/day</u>	
1413	Hair sparse, Shoulder/right 37-86
	Nodule, 1-5 mm, Inguinal region/right 85, 86
	Swelling, Axillary region/left 68-78
	Swelling, Axillary region/right 69-78
1414	No abnormalities detected 1-11
	Hair sparse, Cranial region 12-94
	Hair sparse, Face 49-94
	Swelling, Axillary region/right 90-94
1415	No abnormalities detected 1-10
	Hair sparse, Cervical region 51-98
	Hair sparse, Forefoot/left 39-98
	Hair sparse, Forefoot/right 39-98
	Hair sparse, Forelimb/left 11-98
	Hair sparse, Forelimb/right 11-98
	Hair sparse, Hind limb/left 90-98
	Hair sparse, Hind limb/right 90-98
	Posture hunched 94-98
	Swelling, Axillary region/right 66-73
	Thin 94-98
1416	No abnormalities detected 1-9, 25-32
	Hair sparse, Cervical region 10-24

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number	Week(s) Sign Present
<u>1 mg/kg/day</u>	
1416	Hair sparse, Face 60-96
	Hair sparse, Forefoot/left 33-100
	Hair sparse, Forefoot/right 33-100
	Nodule, 1-5 mm, Axillary region/right 52-100
	Swelling, Cervical region 92-95
1417	No abnormalities detected 1-6, 65, 66
	Hair sparse, Cervical region 37-64
	Hair sparse, Face 7-36
	Nodule, 1-5 mm, Anogenital region 76-89
	Scabbed area, Face 9
	Swelling, Abdominal region 67-85
	Swelling, Inguinal region/left 59, 60
	Swelling, Inguinal region/right 59-64
1418	No abnormalities detected 1-7, 25-67
	Ear/portion of ear missing, Ear/right 68-100
	Hair sparse, Forelimb/right 8-24
	Swelling, Axillary region/left 90-99
1419	No abnormalities detected 1-80, 89-91
	Nodule, 1-5 mm, Axillary region/right 99, 100
	Swelling, Anogenital region 81-88
	Swelling, Axillary region/right 92-100

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number	Week(s) Sign Present
<u>1 mg/kg/day</u>	
1419 Swelling, Cervical region	97-100
Thin	97-100
1420 No abnormalities detected	1-8
Hair sparse, Cervical region	25-62
Hair sparse, Face	9-28
1421 No abnormalities detected	1-32, 36-41, 43
Nodule, 1-5 mm, Axillary region/right	33-35
Scabbed area, Thoracic region	42
1422 No abnormalities detected	1-73
Lacrimation, Eye/left	74-76
Lacrimation, Eye/right	74-76
Piloerection	76, 77
Posture hunched	76, 77
Unkempt appearance	74-77
1423 No abnormalities detected	1-58
Head tilt	63
Piloerection	61-63
Posture hunched	59-63
Thin	60-63
1424 No abnormalities detected	1-100

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number		Week(s) Sign Present
<u>1 mg/kg/day</u>		
1425	No abnormalities detected	1-97
	Ulcer plantar/palmar, 1-5 mm, Hind foot/right	98-100
1426	No abnormalities detected	1-8, 26-36
	Abrasion(s), Face	12, 13
	Activity decreased	77
	Hair sparse, Face	9-25, 37-63
	Nodule, 1-5 mm, Axillary region/left	58-67
	Nodule, 5-20 mm, Axillary region/left	68-73
	Nodule, 5-20 mm, Axillary region/right	68-82
	Posture hunched	80-82
	Scabbed area, Face	14-24
	Swelling, Anogenital region	60-77
	Thin	77-82
1427	No abnormalities detected	1-64
	Ear/portion of ear missing, Ear/right	65-72
1428	No abnormalities detected	1-19
	Hair discolored, Brown, Face	80, 81
	Hair sparse, Face	25-81
	Material around nose, Black	80, 81
	Scabbed area, Face	20-25, 30-32

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number		Week(s) Sign Present
<u>1 mg/kg/day</u>		
1429	No abnormalities detected	1-12
	Hair sparse, Forefoot/left	13-36, 74-100
	Hair sparse, Forefoot/right	13-100
	Material around eyes, Black, Eye/left	55-60, 76, 77
	Material around eyes, Black, Eye/right	76, 77
	Material around eyes, Red, Eye/right	63
	Material around nose, Red	97-100
	Swelling, Anogenital region	90-95
	Swelling, Cervical region	86-94
	Swelling, Inguinal region/left	86-99
1430	No abnormalities detected	1-7
	Hair sparse, Face	8-100
	Hair sparse, Forelimb/left	8-36, 38-100
	Hair sparse, Forelimb/right	13-35
	Hair sparse, Shoulder/right	37-100
	Nodule, 1-5 mm, Anogenital region	92-100
	Nodule, 1-5 mm, Axillary region/left	67-100
	Scabbed area, Face	8-18, 45-51
	Swelling, Inguinal region/right	86-94
1431	No abnormalities detected	1-85
	Swelling, Axillary region/left	86-100

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number	Week(s) Sign Present
<u>1 mg/kg/day</u>	
1431 Ulcer plantar/palmar, 1-5 mm, Hind foot/left	98-100
1432 No abnormalities detected	1-87, 96-100
Swelling, Anogenital region	88-95
1433 No abnormalities detected	1-17
Hair absent, Dorsal surface	77
Hair sparse, Cervical region	27-77
Hair sparse, Cranial region	18-77
Hair sparse, Forefoot/left	19-24
Hair sparse, Forefoot/right	19-24
Hair sparse, Thoracic region	36-77
Hair sparse, Ventral surface	35
Material around eyes, Red, Eye/left	74-76
Material around mouth, Black	76
1434 No abnormalities detected	1-6
Hair sparse, Forelimb/left	7-100
Hair sparse, Forelimb/right	7-100
Nodule, 1-5 mm, Axillary region/right	95-98
Swelling, Anogenital region	86, 87
Swelling, Axillary region/left	86-98
Vocalization	90-94
1435 No abnormalities detected	1-47, 61-75, 85-100

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number	Week(s) Sign Present
<u>1 mg/kg/day</u>	
1435	Nodule, 1-5 mm, Axillary region/right Nodule, 5-20 mm, Axillary region/right Swelling, Thoracic region
	76-83 84 48-60
1436	No abnormalities detected Hair sparse, Cervical region
	1-32 33-89
1437	No abnormalities detected Hair sparse, Cervical region Hair sparse, Face Malocclusion Nodule, 1-5 mm, Anogenital region Scabbed area, Face Swelling, Anogenital region Swelling, Thoracic region Teeth cut
	1-23, 38-42, 72-89 33-36 24-36, 43-71 37, 96-100 92-100 24-27 90, 91 98 37, 90, 91, 94, 96, 98
1438	No abnormalities detected Hair sparse, Face Scabbed area, Face
	1-4, 15, 37-45, 65-100 8-14, 16-36, 46-64 5-10
1439	No abnormalities detected Hair sparse, Abdominal region Material around eyes, Black, Eye/right
	1-65 66-97 96, 97

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number	Week(s) Sign Present
<u>1 mg/kg/day</u>	
1439 Thin	97
1440 No abnormalities detected	1-10, 25-85, 89-100
Hair sparse, Hind limb/right	11-24
Swelling, Anogenital region	86-88
1441 No abnormalities detected	1-24
Hair sparse, Thoracic region	25-74
Scabbed area, Cervical region	27
Scabbed area, Ear/right	27
Scabbed area, Face	39-63
Scabbed area, Thoracic region	38-42
1442 No abnormalities detected	1-7, 82-85
Abrasion(s), Face	66-81
Hair sparse, Face	8-81
Material around eyes, Red, Eye/left	67-76
Material around eyes, Red, Eye/right	67-76
Scabbed area, Face	8-18, 26-32
Swelling, Axillary region/left	42
Swelling, Axillary region/right	30-32
Swelling, Inguinal region/right	43-51
1443 No abnormalities detected	1-36, 84, 85

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number	Week(s) Sign Present
<u>1 mg/kg/day</u>	
1443	Hair sparse, Cervical region 37-83
	Nodule, 1-5 mm, Axillary region/left 49-66
	Nodule, 5-20 mm, Axillary region/left 67-78
	Swelling, Anogenital region 86-88
	Swelling, Axillary region/right 86-88
1444	No abnormalities detected 1-44, 60-65
	Hair sparse, Forefoot/left 45-59
	Nodule, 1-5 mm, Axillary region/left 77
	Nodule, 5-20 mm, Tail 66-77
	Scabbed area, Tail 76, 77
1445	No abnormalities detected 1-54
	Activity decreased 55
	Breathing slow 55
	Eyelid partially/completely closed, Eye/left 55
	Eyelid partially/completely closed, Eye/right 55
	Material around eyes, Black, Eye/left 55
	Posture hunched 55
	Righting reflex impaired 55
1446	No abnormalities detected 1-68
1447	No abnormalities detected 1-17

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number	Week(s) Sign Present
<u>1 mg/kg/day</u>	
1447	Hair sparse, Anogenital region 28-36
	Hair sparse, Cervical region 49-100
	Hair sparse, Shoulder/left 37-100
	Hair sparse, Thoracic region 37-100
	Nodule, 1-5 mm, Anogenital region 92-100
	Nodule, 1-5 mm, Thoracic region 92-100
	Nodule, 5-20 mm, Anogenital region 25-32
	Scabbed area, Cervical region 18-24
	Swelling, Abdominal region 86-91
	Swelling, Anogenital region 90, 91, 98-100
	Swelling, Axillary region/left 95-100
	Swelling, Thoracic region 77-91
1448	No abnormalities detected 1-15, 43-67
	Hair sparse, Cervical region 25-42, 68-86
	Hair sparse, Face 16-37, 39-42
	Malocclusion 19-23
	Teeth cut 19-21
1449	No abnormalities detected 1-42, 46-59, 65-73
	Swelling, Axillary region/left 60-64
	Swelling, Axillary region/right 43-45
1450	No abnormalities detected 1-26, 43-45, 47-73

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number		Week(s) Sign Present
<u>1 mg/kg/day</u>		
1450	Abrasion(s), Thoracic region	46
	Ear/portion of ear missing, Ear/left	74-100
	Hair sparse, Cervical region	28-38
	Hair sparse, Face	39-42
	Hair sparse, Thoracic region	39-42
	Nodule, 1-5 mm, Axillary region/left	92-100
	Scabbed area, Thoracic region	27
1451	No abnormalities detected	1-32, 35, 36, 38, 52-73
	Hair sparse, Cervical region	33, 34, 37
	Posture hunched	89-92
	Swelling, Axillary region/left	39-51
	Swelling, Axillary region/right	74-92
	Thin	89-92
1452	No abnormalities detected	1-61, 74-77
	Nodule, 1-5 mm, Axillary region/right	62-73
	Scabbed area, Axillary region/right	78-80
	Vocalization	70-73
1453	No abnormalities detected	1-36, 52-59
	Hair discolored, Yellow, Anogenital region	60
	Piloerection	60
	Swelling, Anogenital region	37-51

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number	Week(s) Sign Present
<u>1 mg/kg/day</u>	
1454	No abnormalities detected 1-26, 28-89, 99, 100
	Nodule, 1-5 mm, Inguinal region/right 92-94
	Nodule, 5-20 mm, Inguinal region/right 95-98
	Scabbed area, Ear/right 27
	Swelling, Inguinal region/right 90, 91
1455	No abnormalities detected 1-86
1456	No abnormalities detected 1-55, 59-83
	Posture hunched 84
	Scabbed area, Cervical region 84
	Swelling, Cervical region 56-58
1457	No abnormalities detected 1-24, 60-67
	Hair sparse, Cranial region 25-59
	Material around eyes, Black, Eye/left 80, 81
	Scabbed area, Eye/left 80, 81
	Swelling, Axillary region/right 68-81
1458	No abnormalities detected 1-17, 19-25, 36
	Activity decreased 39
	Hair sparse, Face 26-28
	Hair sparse, Hind limb/right 39

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number	Week(s) Sign Present
<u>1 mg/kg/day</u>	
1458	Scabbed area, Ear/left Scabbed area, Face Unkempt appearance
	18 26-35 37-39
1459	No abnormalities detected Activity decreased Hair sparse, Abdominal region Hair sparse, Cervical region Hair sparse, Forefoot/left Hair sparse, Forefoot/right Hair sparse, Forelimb/left Hair sparse, Forelimb/right Hair sparse, Thoracic region Hair sparse, Ventral surface Material around eyes, Red, Eye/left Material around nose, Red Nodule, 1-5 mm, Abdominal region Thin
	1 74 39-59 19-74 2-74 2-74 66-74 66-74 33-59 60-74 74 74 72-74 74
1460	No abnormalities detected Hair sparse, Cervical region Hair sparse, Face Scabbed area, Face Swelling, Axillary region/left
	1-18 28-100 19-96 27 70-85, 90-99

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number	Week(s) Sign Present
<u>1 mg/kg/day</u>	
1461	No abnormalities detected 1-18, 25
	Hair sparse, Cervical region 38-72
	Hair sparse, Forefoot/left 26-72
	Hair sparse, Forefoot/right 26-72
	Hair sparse, Nose/muzzle 19-24
	Hair sparse, Ventral surface 60-72
	Nodule, 1-5 mm, Axillary region/left 62
	Nodule, 1-5 mm, Inguinal region/left 62-65
	Swelling, Axillary region/left 51-62
1462	No abnormalities detected 1-54
	Material around nose, Red 55-58
1463	No abnormalities detected 1-75
	Nodule, 1-5 mm, Axillary region/left 76-88
1464	No abnormalities detected 1-60, 75-78
	Posture hunched 79
	Swelling, Anogenital region 68-74
	Swelling, Axillary region/right 61-73
	Thin 79
1465	No abnormalities detected 1-78

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number		Week(s) Sign Present
<u>1 mg/kg/day</u>		
1466	No abnormalities detected	1-30
1467	No abnormalities detected	1-42, 64-71, 95-100
	Hair sparse, Thoracic region	43-63
	Nodule, 1-5 mm, Thoracic region	72-94
	Swelling, Axillary region/left	80, 81
	Swelling, Inguinal region/right	75-79
1468	No abnormalities detected	1-69
	Hair discolored, Yellow, Anogenital region	78
	Material around nose, Red	76-78
	Piloerection	78
	Posture hunched	76-78
	Swelling, Axillary region/left	70-78
	Thin	76-78
1469	No abnormalities detected	1-96
	Thin	97-100
1470	No abnormalities detected	1-37, 52-59
	Swelling, Axillary region/right	38-51
	Swelling, Inguinal region/left	60-62
1471	No abnormalities detected	1-4

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number		Week(s) Sign Present
<u>1 mg/kg/day</u>		
1471	Hair absent, Dorsal surface	98-100
	Hair sparse, Forelimb/left	18-100
	Hair sparse, Forelimb/right	18-100
	Hair sparse, Hind limb/left	19-100
	Hair sparse, Hind limb/right	19-100
	Hair sparse, Ventral surface	13-100
	Malocclusion	5-100
	Nodule, 1-5 mm, Ventral surface	65-100
	Teeth broken	5-13
	Teeth cut	45, 46, 78
1472	No abnormalities detected	1-26, 29-32, 64-68
	Carriage high	85
	Hair sparse, Cervical region	27, 28, 33-63, 69-85
	Posture hunched	85
	Swelling, Anogenital region	73-78
	Thin	85
1473	No abnormalities detected	1-18, 64, 65, 79-89
	Hair sparse, Cervical region	25-63
	Hair sparse, Face	19-24
	Hair sparse, Ventral surface	90-92
	Nodule, 1-5 mm, Mouth	66-73
	Swelling, Anogenital region	49-63

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number	Week(s) Sign Present
<u>1 mg/kg/day</u>	
1473 Swelling, Axillary region/left	67-78
1474 No abnormalities detected	1-18
Hair sparse, Cervical region	33-51
Hair sparse, Face	19-42
Head tilt	46-51
Leaning	49-51
Material around eyes, Black, Eye/left	47-50
Righting reflex impaired	49-51
1475 No abnormalities detected	1-67, 70-73, 75-78, 86-94
Material around eyes, Black, Eye/left	74
Material around eyes, Red, Eye/right	68, 69
Skin discolored, Black, Anogenital region	95-100
Swelling, Anogenital region	79-85
1476 No abnormalities detected	1-24, 38-87
Hair sparse, Cervical region	25-37
1477 No abnormalities detected	1-84
Hair discolored, Red, Face	85, 86
1478 No abnormalities detected	1-42, 51-61, 79-89
Hair sparse, Ventral surface	90

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number	Week(s) Sign Present
<u>1 mg/kg/day</u>	
1478 Nodule, 1-5 mm, Axillary region/left	62-74
Swelling, Anogenital region	43-50
Swelling, Axillary region/right	72-78
1479 No abnormalities detected	1-17, 78-89
Hair sparse, Face	19-77
Hair sparse, Forelimb/right	18-38
Nodule, 1-5 mm, Thoracic region	90
1480 No abnormalities detected	1-17
Activity decreased	77
Hair sparse, Forefoot/left	18-77
Hair sparse, Forefoot/right	18-77
Thin	77
<u>50 mg/kg/day</u>	
1481 No abnormalities detected	1-31, 40, 41, 44-52
Hair sparse, Face	32-39, 42, 43
1482 No abnormalities detected	1-52
1483 No abnormalities detected	1-13, 16-38
Hair sparse, Hind limb/left	14, 15

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number	Week(s) Sign Present
<u>50 mg/kg/day</u>	
1483 Hair sparse, Thoracic region	39-52
1484 No abnormalities detected	1-11, 29-52
Hair sparse, Face	12-28
1485 No abnormalities detected	1-52
1486 No abnormalities detected	1-37
Hair sparse, Face	44-52
Nodule, 1-5 mm, Axillary region/right	38, 39
Swelling, Anogenital region	40-52
1487 No abnormalities detected	1-33
Hair sparse, Thoracic region	34-52
1488 No abnormalities detected	1-4
Hair sparse, Cervical region	5-14, 20-52
Hair sparse, Dorsal surface	10-13, 15-33
Hair sparse, Forefoot/left	34-52
Hair sparse, Forefoot/right	34-52
Hair sparse, Lumbar region	38
Hair sparse, Shoulder/left	42-51
Hair sparse, Shoulder/right	42-52
Hair sparse, Thoracic region	5-14, 34-38

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number	Week(s) Sign Present
<u>50 mg/kg/day</u>	
1488	Nodule, 1-5 mm, Axillary region/left Scabbed area, Inguinal region/right Swelling, Axillary region/left 48-50 51, 52 51, 52
1489	No abnormalities detected 1-52
1490	No abnormalities detected Swelling, Axillary region/right 1-33, 43-52 34-42
1491	No abnormalities detected Abrasion(s), Abdominal region Swelling, Cervical region Swelling, Inguinal region/left 1-59 96-100 60-100 68-87
1492	No abnormalities detected 1-73
1493	No abnormalities detected Hair sparse, Cervical region Hair sparse, Face Hair sparse, Thoracic region Posture hunched Scabbed area, Face 1-27 28-66 34-66 34-66 63-66 36-38
1494	No abnormalities detected 1-50, 58, 59, 95-99

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number	Week(s) Sign Present
<u>50 mg/kg/day</u>	
1494	Hair sparse, Cervical region 60-87 Material around eyes, Black, Eye/left 100 Swelling, Anogenital region 51-57, 65-94
1495	No abnormalities detected 1-24, 32-84 Nodule, 1-5 mm, Axillary region/right 85-93 Stereotypy, Straub tail 25-31
1496	No abnormalities detected 1-28 Hair absent, Dorsal surface 79-100 Hair discolored, Yellow, Anogenital region 96-99 Hair sparse, Cervical region 29-91 Hair sparse, Face 42-51 Hair sparse, Thoracic region 34-78 Hair wet, Anogenital region 96-99 Scabbed area, Thoracic region 38
1497	No abnormalities detected 1-4, 14, 37-39 Hair sparse, Face 16-36 Hair sparse, Forefoot/left 5-13, 15-36, 40-56 Hair sparse, Forefoot/right 5-13, 15-36
1498	No abnormalities detected 1-3 Hair sparse, Forefoot/left 4-54

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number	Week(s) Sign Present
<u>50 mg/kg/day</u>	
1498	Hair sparse, Forefoot/right Hair sparse, Forelimb/left Hair sparse, Forelimb/right
	4-54 39-54 39-54
1499	No abnormalities detected Hair sparse, Face Nodule, 1-5 mm, Axillary region/left Swelling, Axillary region/left Thin
	1-6, 14-53, 60-87 7-13 58, 59 54-59 88
1500	No abnormalities detected
	1-100
1501	No abnormalities detected Hair sparse, Anogenital region Material around nose, Brown Swelling, Anogenital region
	1-37, 39-59 38 61 60, 61
1502	No abnormalities detected Material around eyes, Red, Eye/left Nodule, 1-5 mm, Axillary region/right Swelling, Anogenital region
	1-33, 42-73, 95-100 34-41 88-94 74-87
1503	No abnormalities detected Hair sparse, Thoracic region
	1-37, 52-77, 79-91 38-51

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number	Week(s) Sign Present
<u>50 mg/kg/day</u>	
1503 Material around nose, Red	78
1504 No abnormalities detected	1-60
Head tilt	61-64
Righting reflex impaired	61
Thin	63, 64
1505 No abnormalities detected	1-33
Hair sparse, Cervical region	38-84
Hair sparse, Face	34-84
Hair sparse, Thoracic region	34-84
Nodule, 1-5 mm, Cervical region	73
Nodule, 1-5 mm, Inguinal region/right	62
Nodule, 5-20 mm, Cervical region	74-78
1506 No abnormalities detected	1-33, 37-62
Swelling, Thoracic region	34-36
1507 No abnormalities detected	1-59
Activity decreased	60
1508 No abnormalities detected	1-10, 88
Hair sparse, Cervical region	16-87
Hair sparse, Cranial region	11-13

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number		Week(s) Sign Present
<u>50 mg/kg/day</u>		
1508	Hair sparse, Face	14-87
	Swelling, Thoracic region	43-59
1509	No abnormalities detected	1-53, 72-84
	Hair sparse, Abdominal region	85-92
	Swelling, Axillary region/right	54-71
1510	No abnormalities detected	1-67
1511	No abnormalities detected	1-76
	Material around eyes, Black, Eye/left	77
1512	No abnormalities detected	1-37
1513	No abnormalities detected	1-26, 35-37, 39, 40
	Hair sparse, Cervical region	29-34
	Hair sparse, Thoracic region	38
	Laceration, Cervical region	27
	Scabbed area, Cervical region	28
1514	No abnormalities detected	1-52
	Activity decreased	56
	Carriage high	54, 55
	Inappetence	56

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number	Week(s) Sign Present
<u>50 mg/kg/day</u>	
1514	Material around nose, Brown Thin
	53-55 53-56
1515	No abnormalities detected Hair sparse, Thoracic region Nodule, 1-5 mm, Cervical region Skin discolored, Pale, Entire body Swelling, Cervical region
	1-23, 34-37 38-76 33 76 24-33
1516	No abnormalities detected Discharge, Red, Vulva Hair sparse, Face Swelling, Anogenital region Ulcer plantar/palmar, 1-5 mm, Hind foot/left Ulcer plantar/palmar, 1-5 mm, Hind foot/right
	1-33, 60-84 96, 100 34-59 85-100 88-100 88-100
1517	No abnormalities detected Hair sparse, Dorsal surface Hair sparse, Forefoot/left Hair sparse, Forefoot/right Nodule, 1-5 mm, Forelimb/left Nodule, 1-5 mm, Thoracic region Swelling, Cervical region Ulcer, 5-20 mm, Cervical region
	1-11 23-33 12-78 12-78 64-67 60-78 43-66 78

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number	Week(s) Sign Present
<u>50 mg/kg/day</u>	
1518 No abnormalities detected	1-24
1519 No abnormalities detected	1-62, 66-78
Posture hunched	79
Swelling, Axillary region/right	63-65
Thin	79
1520 No abnormalities detected	1-45, 59-96
Hair sparse, Face	46-58
Swelling, Axillary region/left	97-100
1521 No abnormalities detected	1-28, 39, 60-65, 80-87
Hair sparse, Forefoot/left	29-38, 40-59
Hair sparse, Forefoot/right	29-38, 40-59
Swelling, Axillary region/right	79
Swelling, Inguinal region/right	66-79
1522 No abnormalities detected	1-6, 14-66, 68-80
Activity decreased	81
Breathing shallow	81
Hair sparse, Face	7-13
Material around eyes, Red, Eye/left	81
Posture hunched	81

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number	Week(s) Sign Present
<u>50 mg/kg/day</u>	
1522	81
Skin cold to touch, Entire body	67
Swelling, Anogenital region	81
Thin	
1523	1-21
No abnormalities detected	22-87
Hair sparse, Face	76-88
Nodule, 1-5 mm, Axillary region/right	22-28
Scabbed area, Face	86, 87
Swelling, Anogenital region	66-75
Swelling, Axillary region/left	
1524	1-3, 11-13, 39-51
No abnormalities detected	17-38
Hair sparse, Face	52-77
Hair sparse, Thoracic region	4-10
Material around eyes, Red, Eye/left	14-16
Scabbed area, Face	72-76
Swelling, Axillary region/left	74-77
Swelling, Thoracic region	
1525	1-59
No abnormalities detected	60-74
Nodule, 1-5 mm, Thoracic region	74
Swelling, Axillary region/left	
1526	1-75, 86-95
No abnormalities detected	

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number	Week(s) Sign Present
<u>50 mg/kg/day</u>	
1526	Activity decreased 96
	Breathing difficult 96
	Moribund 96
	Nodule, 1-5 mm, Anogenital region 76-85
	Righting reflex impaired 96
	Swelling, Abdominal region 82-85
1527	No abnormalities detected 1-39
	Hair sparse, Cervical region 40-87
	Hair sparse, Thoracic region 46-88
	Nodule, 1-5 mm, Ear/left 70-81
	Nodule, 5-20 mm, Ear/left 82-88
	Swelling, Anogenital region 74-79
1528	No abnormalities detected 1-37, 39-63, 92-96
	Hair sparse, Cervical region 77-91
	Material around nose, Black 38
	Nodule, 1-5 mm, Inguinal region/right 64-85
	Thin 97-100
1529	No abnormalities detected 1-37, 46-55
	Hair sparse, Forefoot/left 38-45, 56-63
	Hair sparse, Forefoot/right 38-45, 56-63
1530	No abnormalities detected 1-32, 60-71, 77

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number	Week(s) Sign Present
<u>50 mg/kg/day</u>	
1530	Hair sparse, Face 33-59
	Material in nares 72
	Scabbed area, Face 33-40
	Swelling, Axillary region/left 72-76
1531	No abnormalities detected 1-67, 77, 78
	Material around nose, Red 84, 85
	Swelling, Axillary region/left 79-85
	Swelling, Inguinal region/right 68-76
1532	No abnormalities detected 1-24, 92-97
	Hair sparse, Face 35-91
	Hair sparse, Forelimb/right 37-91
	Hair sparse, Thoracic region 25-91
	Swelling, Axillary region/left 98, 99
	Swelling, Axillary region/right 100
1533	No abnormalities detected 1-41
	Hair sparse, Face 42-80
	Nodule, 1-5 mm, Shoulder/left 58, 59
	Swelling, Axillary region/left 60-64
1534	No abnormalities detected 1-73
	Hair sparse, Forefoot/right 74-83

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number	Week(s) Sign Present
<u>50 mg/kg/day</u>	
1535	No abnormalities detected 1-44, 46-74
	Material in pan/bedding, Red 75
	Swelling, Cervical region 45
1536	No abnormalities detected 1-28
	Activity decreased 55
	Hair sparse, Cervical region 39-55
	Hair sparse, Face 30-55
	Hair sparse, Forefoot/left 34-55
	Hair sparse, Forefoot/right 34-55
	Hair sparse, Ventral surface 29-55
1537	No abnormalities detected 1-9, 11-48
	Abrasion(s), Face 66-81
	Hair sparse, Cervical region 52-81
	Hair sparse, Face 49-81
	Material around nose, Brown 79-81
	Scabbed area, Cervical region 10, 52-59, 67-81
	Scabbed area, Face 49-59
1538	No abnormalities detected 1-13, 60-76
	Hair discolored, Yellow, Ventral surface 77-100
	Hair sparse, Cervical region 14-59

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number	Week(s) Sign Present
<u>50 mg/kg/day</u>	
1538	Hair wet, Anogenital region 96-99
	Ulcer plantar/palmar, 1-5 mm, Hind foot/left 100
1539	No abnormalities detected 1-65
	Abrasion(s), Cranial region 75
	Breathing audible 74
	Material around eyes, Red, Eye/right 75
	Scabbed area, Ear/right 72, 73
	Swelling, Axillary region/left 68-75
	Swelling, Axillary region/right 66, 67
	Swelling, Cranial region 75
1540	No abnormalities detected 1-59, 88, 89
	Hair sparse, Cervical region 60-87
	Swelling, Axillary region/right 79-87
	Swelling, Inguinal region/left 85-87
	Swelling, Inguinal region/right 85
1541	No abnormalities detected 1, 2
	Hair sparse, Forefoot/left 3-100
	Hair sparse, Forefoot/right 3-100
	Hair sparse, Forelimb/left 34-100
	Hair sparse, Forelimb/right 34-100
	Hair sparse, Thoracic region 68-100

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number	Week(s) Sign Present
<u>50 mg/kg/day</u>	
1541	Hair sparse, Ventral surface 85-100 Swelling, Axillary region/right 91-100
1542	No abnormalities detected 1-26 Hair sparse, Cervical region 29-45 Hair sparse, Forelimb/right 33 Hair sparse, Shoulder/right 33-45 Scabbed area, Face 27, 28
1543	No abnormalities detected 1-100
1544	No abnormalities detected 1-18 Activity decreased 75 Hair sparse, Face 19-38 Nodule, 1-5 mm, Nose/muzzle 35-75 Posture hunched 75 Thin 75
1545	No abnormalities detected 1-47
1546	No abnormalities detected 1-28 Eye discolored, Pale, Eye/left 32, 33 Eye discolored, Pale, Eye/right 32, 33 Hair sparse, Forefoot/left 38-100

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number	Week(s) Sign Present
<u>50 mg/kg/day</u>	
1546	Hair sparse, Forefoot/right 38-100 Hair sparse, Thoracic region 29-87
1547	No abnormalities detected 1-100
1548	No abnormalities detected 1-19, 39-65 Hair sparse, Abdominal region 66-88 Hair sparse, Face 20-38 Swelling, Anogenital region 68-79
1549	No abnormalities detected 1-53, 92-95 Hair sparse, Forefoot/left 54-91 Hair sparse, Forefoot/right 54-91 Swelling, Anogenital region 96-99 Swelling, Axillary region/right 97-100
1550	No abnormalities detected 1-67, 74, 75, 86, 87 Hair sparse, Cranial region 68-73 Nodule, 1-5 mm, Axillary region/left 88-90 Nodule, 1-5 mm, Inguinal region/left 76-85
1551	No abnormalities detected 1-29 Carriage high 67 Hair sparse, Forefoot/left 30-67

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number	Week(s) Sign Present
<u>50 mg/kg/day</u>	
1551	Hair sparse, Forefoot/right 30-67
	Hair sparse, Forelimb/left 34-39
	Hair sparse, Forelimb/right 34-39
	Inappetence 67
	Piloerection 67
	Posture hunched 67
	Thin 67
1552	No abnormalities detected 1-33
	Hair sparse, Cervical region 34-51
	Hair sparse, Face 38
	Head tilt 51
1553	No abnormalities detected 1-100
1554	No abnormalities detected 1-68
	Head tilt 69
1555	No abnormalities detected 1-11
	Hair sparse, Cervical region 20-46
	Hair sparse, Cranial region 29-46
	Hair sparse, Face 12-28, 42-46
	Scabbed area, Face 12-16
1556	No abnormalities detected 1-33

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number	Week(s) Sign Present
<u>50 mg/kg/day</u>	
1556	Hair sparse, Forefoot/left Hair sparse, Forefoot/right Nodule, 1-5 mm, Cervical region Skin discolored, Black, Anogenital region Swelling, Anogenital region
	34-50 34-50 48-50 38-50 46-48
1557	No abnormalities detected Material around nose, Black
	1-93 94
1558	No abnormalities detected Nodule, 1-5 mm, Axillary region/left Nodule, 5-20 mm, Axillary region/left
	1-72, 75-88 73 74
1559	No abnormalities detected Swelling, Inguinal region/right
	1-83, 88-100 84-87
1560	No abnormalities detected Material around nose, Black Swelling, Anogenital region Swelling, Cervical region
	1-43 67-80 52-80 44-53
<u>500 mg/kg/day</u>	
1561	No abnormalities detected
	1-23, 34-51

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number	Week(s) Sign Present
<u>500 mg/kg/day</u>	
1561	Hair sparse, Forefoot/left 52 Hair sparse, Forelimb/left 24-33
1562	No abnormalities detected 1-4, 6 Hair sparse, Face 7-31 Hair sparse, Forefoot/left 26-52 Hair sparse, Forefoot/right 28-52 Posture hunched 51, 52 Salivation 5, 7, 38-50
1563	No abnormalities detected 1-52
1564	No abnormalities detected 1-22, 42-52 Hair sparse, Face 25-28 Hair sparse, Forefoot/left 23-41 Hair sparse, Forefoot/right 23-33
1565	No abnormalities detected 1-33 Hair sparse, Forelimb/left 34-52 Hair sparse, Forelimb/right 34-52 Hair sparse, Hind limb/left 38-52
1566	No abnormalities detected 1-33 Hair sparse, Cervical region 37-49

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number	Week(s) Sign Present
<u>500 mg/kg/day</u>	
1566	Hair sparse, Cranial region 38-49
	Hair sparse, Shoulder/right 40-49
	Salivation 34-41
1567	No abnormalities detected 1-12
	Hair sparse, Abdominal region 31-37
	Hair sparse, Cervical region 13-49
	Hair sparse, Forefoot/left 29-49
	Hair sparse, Forefoot/right 29-49
	Hair sparse, Shoulder/right 25-49
	Hair sparse, Ventral surface 38-49
	Scabbed area, Inguinal region/right 32-48
	Swelling, Anogenital region 38-49
1568	No abnormalities detected 1-27
	Hair sparse, Forefoot/left 28-52
	Hair sparse, Forefoot/right 28-52
	Salivation 28-33, 39-50
	Swelling, Anogenital region 45-48
1569	No abnormalities detected 1-24, 31-48, 52
	Hair sparse, Thoracic region 25-30
	Swelling, Anogenital region 49-51
1570	No abnormalities detected 1-6, 8-24, 26, 27, 29-37, 42-52

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number	Week(s) Sign Present
<u>500 mg/kg/day</u>	
1570	28
Hair sparse, Forefoot/left	28
Hair sparse, Forefoot/right	7, 25, 28, 38-41
Salivation	
1571	1-12
No abnormalities detected	13-52
Hair sparse, Forefoot/left	13-52
Hair sparse, Forefoot/right	
1572	1-11, 32-39
No abnormalities detected	12-31
Hair sparse, Face	12-21
Hair sparse, Forefoot/left	12-21, 40-52
Hair sparse, Forefoot/right	
1573	1-67, 77-87
No abnormalities detected	97
Discharge, Clear, Vulva	97
Material around nose, Red	90-97
Nodule, 1-5 mm, Axillary region/right	88-91
Nodule, 1-5 mm, Thoracic region	68-76
Swelling, Inguinal region/right	
1574	1-73
No abnormalities detected	
1575	1-24, 60-73
No abnormalities detected	25-59
Hair sparse, Face	

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number	Week(s) Sign Present
<u>500 mg/kg/day</u>	
1575 Scabbed area, Face	25-38
1576 No abnormalities detected	1-83, 86-96
Swelling, Inguinal region/left	84, 85
Thin	97-100
1577 No abnormalities detected	1-37, 50-52
Hair discolored, Tan, Ventral surface	39-49
Hair discolored, Yellow, Anogenital region	53-86
Nodule, 1-5 mm, Inguinal region/left	66-86
Salivation	38, 39
Swelling, Anogenital region	80-86
Swelling, Thoracic region	72-86
1578 No abnormalities detected	1-27, 31, 32
Abrasion(s), Periocular/left	44-58
Hair discolored, Tan, Ventral surface	39-100
Laceration, Eyelid/left	33-41
Laceration, Periocular/left	28-30
Salivation	89, 90
1579 No abnormalities detected	1-5, 11-21
Hair sparse, Anogenital region	68-87
Hair sparse, Cervical region	27-59

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number	Week(s) Sign Present
<u>500 mg/kg/day</u>	
1579	Hair sparse, Dorsal surface 40-59
	Hair sparse, Forefoot/left 22-87
	Hair sparse, Forefoot/right 22-87
	Hair sparse, Forelimb/left 29-87
	Hair sparse, Hind foot/left 27, 28
	Hair sparse, Mouth 7-10
	Hair sparse, Ventral surface 29-87
	Scabbed area, Mouth 6
	Swelling, Axillary region/right 63-65
1580	No abnormalities detected 1-28
	Hair sparse, Cervical region 32-50
	Hair sparse, Cranial region 34-50
	Hair sparse, Face 29-50
	Salivation 39-41
1581	No abnormalities detected 1-3, 18-27, 29-100
	Hair sparse, Face 16, 17
	Salivation 4-15, 28
	Scabbed area, Face 10-17
1582	No abnormalities detected 1-24, 60-73
	Hair sparse, Face 39-59
	Hair sparse, Forefoot/left 28-33, 37-59

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number	Week(s) Sign Present
<u>500 mg/kg/day</u>	
1582	Hair sparse, Forefoot/right Posture hunched Thin
	25-59, 74-89 89 89
1583 ^r	No abnormalities detected Hair discolored, Yellow, Anogenital region Hair sparse, Forefoot/right Salivation Skin discolored, Black, Anogenital region Skin discolored, Black, Axillary region/right Swelling, Axillary region/left Swelling, Axillary region/right
	1-24, 27-37 56 38-56 25, 26, 38-50 56 56 52, 53 38-46
1584 ^r	No abnormalities detected Salivation
	1-6, 10-23, 32-37, 42-47, 51-76 7-9, 24-31, 38-41, 48-50
1585	No abnormalities detected
	1-100
1586	No abnormalities detected Hair sparse, Forefoot/left Hair sparse, Forefoot/right
	1-18, 60-84 19-59 19-59
1587	No abnormalities detected Nodule, 5-20 mm, Anogenital region
	1-38, 42-88 89-100

^r Replacement animal

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number	Week(s) Sign Present
<u>500 mg/kg/day</u>	
1587	Salivation 39-41, 90-100 Swelling, Cervical region 92-100
1588	No abnormalities detected 1-9, 29-34, 52-66 Hair discolored, Yellow, Anogenital region 67-80 Hair sparse, Forefoot/left 10-28 Hair sparse, Forefoot/right 10-28 Material around eyes, Red, Eye/left 35-37 Swelling, Axillary region/right 38-51
1589	No abnormalities detected 1-28, 30-42, 51-60, 62-72 Hair discolored, Brown, Ventral surface 47-49 Hair discolored, Tan, Ventral surface 73-80 Material around eyes, Black, Eye/right 29 Posture hunched 78-80 Salivation 43-50, 61 Thin 78-80
1590	No abnormalities detected 1-24, 82-84 Hair discolored, Yellow, Anogenital region 57-76 Hair sparse, Forefoot/left 25-76 Hair sparse, Forefoot/right 25-76 Swelling, Inguinal region/right 68-81
1591	No abnormalities detected 1-3, 11, 22-24, 26, 31-38, 42-84

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number	Week(s) Sign Present
<u>500 mg/kg/day</u>	
1591	28
Hair sparse, Face	27
Material around eyes, Red, Eye/right	4-10, 12-21, 25, 27-30, 39-41
Salivation	
1592	1-3, 11-24, 27, 31-38, 60-82, 88, 89
No abnormalities detected	39-59
Hair sparse, Cervical region	4
Material around eyes, Red, Eye/left	90
Nodule, 1-5 mm, Axillary region/right	5-10, 28-30
Salivation	25, 26
Scabbed area, Abdominal region	83-87
Swelling, Inguinal region/right	4, 5
Teeth broken	
1593	1-10, 74, 77
No abnormalities detected	92-100
Eye discolored, White, Eye/left	96-100
Hair discolored, Brown, Ventral surface	11-73
Hair sparse, Forefoot/left	11-13, 16-33, 38-73
Hair sparse, Forefoot/right	78-100
Material around eyes, Black, Eye/left	60
Material around eyes, Red, Eye/left	99, 100
Swelling, Anogenital region	75, 76, 100
Teeth cut	
1594	1-100
No abnormalities detected	

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number		Week(s) Sign Present
<u>500 mg/kg/day</u>		
1595	No abnormalities detected	1-6, 10-14, 88, 89, 91-96
	Eye protruding, Eye/left	97-100
	Eye protruding, Eye/right	97-100
	Hair sparse, Cranial region	28-78
	Hair sparse, Dorsal surface	49-87
	Material around eyes, Black, Eye/left	17, 18
	Material around eyes, Red, Eye/left	16
	Salivation	7-9, 15-28, 40-50
	Scabbed area, Cranial region	29, 30
	Teeth cut	60, 90, 97-100
1596	No abnormalities detected	1-32
	Hair sparse, Anogenital region	40-55
	Hair sparse, Forefoot/right	33-55
	Hair sparse, Forelimb/right	34-55
	Hair sparse, Hind limb/left	40-55
	Thin	55
1597	No abnormalities detected	1-38, 42-87
	Material around nose, Red	88-92
	Nodule, 5-20 mm, Inguinal region/left	89, 90
	Salivation	39-41
1598	No abnormalities detected	1-71, 73

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number	Week(s) Sign Present
<u>500 mg/kg/day</u>	
1598	Hair discolored, Brown, Ventral surface 81-84
	Hair wet, Ventral surface 77-84
	Posture hunched 82-84
	Salivation 72, 76-84
	Thin 82-84
	Unkempt appearance 74-84
1599	No abnormalities detected 1-66
	Hair discolored, Yellow, Anogenital region 67-82
	Hypersensitive to touch 67-71
1600	No abnormalities detected 1-27, 88-95
	Breathing audible 97-99
	Hair discolored, Brown, Ventral surface 96-99
	Hair sparse, Cervical region 28
	Hair sparse, Cranial region 34-87
	Hair sparse, Face 29-87
	Hair wet, Ventral surface 79-81
	Swelling, Cervical region 62-66
1601	No abnormalities detected 1-24, 60-62
	Hair sparse, Axillary region/left 63-68
	Hair sparse, Cervical region 63-68
	Hair sparse, Forefoot/left 25-59

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number	Week(s) Sign Present
<u>500 mg/kg/day</u>	
1601	Hair sparse, Forefoot/right Hair sparse, Forelimb/left Hair sparse, Shoulder/left Swelling, Inguinal region/left
	25-59 40-59 63-68 67
1602	No abnormalities detected Activity decreased Hair sparse, Face Hair sparse, Forefoot/left Hair sparse, Forefoot/right Hair sparse, Forelimb/right Lacrimation, Eye/right Salivation Scabbed area, Face
	1-3, 34-37, 60, 67-71 84 4-33 38-59 38-59 72-84 28 24, 25, 40, 41, 61-66 6-13, 20-28
1603	No abnormalities detected Hair sparse, Forefoot/left Hair sparse, Forefoot/right Hair sparse, Forelimb/left Hair sparse, Forelimb/right Hair sparse, Thoracic region Nodule, 1-5 mm, Anogenital region Salivation Scabbed area, Thoracic region
	1-15 67-88 67-88 67-88 67-88 25-88 49 16-28, 48-60, 72, 78-87 32-51

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number	Week(s) Sign Present
<u>500 mg/kg/day</u>	
1603	Swelling, Anogenital region Swelling, Cervical region
	50, 51 78-81
1604	No abnormalities detected Hair sparse, Cranial region Hair sparse, Face Hair sparse, Thoracic region Salivation Scabbed area, Face Swelling, Axillary region/right
	1-9 39-57 10-57 39-57 25 10-14 56, 57
1605	No abnormalities detected Hair discolored, Tan, Ventral surface Hair sparse, Anogenital region Hair sparse, Forefoot/left Hair sparse, Forefoot/right Head tilt Salivation Swelling, Anogenital region
	1-9, 11-14 40-72 15-72 38-72 38-72 72 10, 35, 36, 48-50 68-72
1606	No abnormalities detected Activity decreased Hair sparse, Cervical region Hair sparse, Shoulder/right
	1-5 68 7-68 7-68

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number	Week(s) Sign Present
<u>500 mg/kg/day</u>	
1606	25-68
Hair sparse, Thoracic region	48-51
Nodule, 1-5 mm, Thoracic region	68
Posture hunched	6-10, 13-25, 28-36, 38-50
Salivation	68
Thin	
1607	1-41
No abnormalities detected	97-100
Eye discolored, White, Eye/right	90-100
Eye protruding, Eye/left	90-100
Eye protruding, Eye/right	42-100
Hair discolored, Yellow, Anogenital region	96-100
Swelling, Axillary region/right	
1608	1-38, 60-67
No abnormalities detected	39-59
Hair sparse, Forelimb/left	39-59
Hair sparse, Hind limb/left	68-75
Swelling, Axillary region/right	
1609	1-28, 32-91, 96-98
No abnormalities detected	29-31
Salivation	92-95
Swelling, Anogenital region	
1610	1-23, 26-41
No abnormalities detected	42-45
Hair discolored, Yellow, Anogenital region	

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number	Week(s) Sign Present
<u>500 mg/kg/day</u>	
1610	25
Hair sparse, Forefoot/right	42-45
Piloerection	42-45
Posture hunched	24
Salivation	42-45
Thin	
1611	1-22
No abnormalities detected	23-31, 68-88
Hair sparse, Forefoot/left	32-88
Hair sparse, Forefoot/right	74-85
Swelling, Anogenital region	83-85
Swelling, Inguinal region/left	
1612	1-6, 13-24, 26-31, 33-88, 93-100
No abnormalities detected	7-12
Hair sparse, Face	32
Material around eyes, Red, Eye/left	7-12, 25, 89-92
Salivation	
1613	1-6, 95-100
No abnormalities detected	10-87
Hair sparse, Cranial region	25-87
Hair sparse, Face	7-94
Hair sparse, Forefoot/left	7-94
Hair sparse, Forefoot/right	79-88
Swelling, Inguinal region/left	91
Swelling, Inguinal region/right	

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number	Week(s) Sign Present
<u>500 mg/kg/day</u>	
1614	No abnormalities detected 1-4
	Hair sparse, Forefoot/left 6-58
	Hair sparse, Forefoot/right 6-58
	Salivation 5, 13, 39-41
1615	No abnormalities detected 1-14
	Hair discolored, Tan, Ventral surface 39-78
	Hair sparse, Forefoot/left 15-78
	Hair sparse, Forefoot/right 15-78
	Hair sparse, Forelimb/left 34-78
	Hair sparse, Forelimb/right 34-78
	Nodule, 1-5 mm, Anogenital region 76-78
1616	No abnormalities detected 1-13
	Hair discolored, Tan, Ventral surface 39-82
	Hair sparse, Cervical region 14-82
	Hair sparse, Shoulder/left 14-82
	Hair sparse, Shoulder/right 19-82
	Swelling, Cervical region 74-82
1617	No abnormalities detected 1-4, 22, 23, 26-31
	Hair discolored, Brown, Anogenital region 55-57
	Hair sparse, Forefoot/left 32-57

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number	Week(s) Sign Present
<u>500 mg/kg/day</u>	
1617	Hair sparse, Forefoot/right Salivation Swelling, Axillary region/right
	32-57 5-21, 24, 25, 37, 38 48-57
1618	No abnormalities detected Hair sparse, Cervical region Hair sparse, Face Salivation Scabbed area, Face Teeth cut
	1-5, 60-88, 90-99 27-59 6-59 40-50, 89 25, 26 100
1619	No abnormalities detected Swelling, Axillary region/right Swelling, Inguinal region/left
	1-73, 82, 83, 86-96 74-81 84, 85
1620	No abnormalities detected Salivation
	1-38, 42-51, 54-72, 74-90 39-41, 52, 53, 73
1621	No abnormalities detected Salivation Tail missing - portion
	1-5, 11-15, 26, 32-37, 54-69 6-10, 16-25, 27-31, 38-53, 76-87 70-100
1622	No abnormalities detected Salivation
	1-26, 32-75, 88-95 27-31

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number	Week(s) Sign Present
<u>500 mg/kg/day</u>	
1622 Swelling, Anogenital region	76-87
1623 No abnormalities detected	1-39
Hair sparse, Cranial region	42-94
Hair sparse, Face	45-94
Hair sparse, Thoracic region	40-59
Nodule, 1-5 mm, Lumbar region	88-100
1624 No abnormalities detected	1-6
Hair sparse, Face	7-84
Hair sparse, Forefoot/left	39-84
Hair sparse, Forefoot/right	39-84
Hair sparse, Forelimb/left	39-84
Hair sparse, Forelimb/right	39-84
Hair sparse, Ventral surface	40-84
Head tilt	84
Nodule, 1-5 mm, Axillary region/right	78-84
Salivation	12-24
Swelling, Cervical region	80-82
1625 No abnormalities detected	1-31
Hair sparse, Abdominal region	72-82
Hair sparse, Cervical region	32-82
Hair sparse, Shoulder/right	32-82

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number	Week(s) Sign Present
<u>500 mg/kg/day</u>	
1626	No abnormalities detected Salivation Scabbed area, Thoracic region Swelling, Thoracic region
	1-5, 11-23, 26-31, 35-38, 42-62, 67-73, 84 6-10, 24, 25, 32-34, 39-41, 63-66, 76 82, 83 74-81
1627	No abnormalities detected Nodule, 1-5 mm, Axillary region/right Swelling, Axillary region/right
	1-46, 49-56 48 47, 48
1628	No abnormalities detected
	1-100
1629	No abnormalities detected Discharge, Red, Vulva Hair discolored, Yellow, Anogenital region Hair sparse, Forefoot/left Hair sparse, Forefoot/right Salivation
	1-21, 26-38 83 84-90 39-90 56-90 22-25, 39-41
1630	No abnormalities detected Hair sparse, Forefoot/left Hair sparse, Forelimb/left
	1-36 37-90 41-90
1631	No abnormalities detected
	1-3, 32-94

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number	Week(s) Sign Present
<u>500 mg/kg/day</u>	
1631	Eye protruding, Eye/left 97-100
	Eye protruding, Eye/right 97-100
	Hair sparse, Cervical region 95-100
	Hair sparse, Face 4-22
	Hair sparse, Forefoot/left 25-31
	Hair sparse, Thoracic region 14-31
	Scabbed area, Face 4-13
1632	No abnormalities detected 1-3
	Hair sparse, Abdominal region 25-28
	Hair sparse, Cervical region 4-100
	Hair sparse, Inguinal region/right 19, 32-39
	Hair sparse, Lumbar region 7-13
	Hair sparse, Shoulder/left 7-100
	Hair sparse, Shoulder/right 7-100
	Teeth cut 100
1633	No abnormalities detected 1-73, 77-87
	Body rigid 74-76
	Nodule, 5-20 mm, Inguinal region/right 89-91
	Thin 88-100
1634	No abnormalities detected 1-51, 63-71, 73, 88-90
	Swelling, Anogenital region 52-62, 72, 74-87

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number		Week(s) Sign Present
<u>500 mg/kg/day</u>		
1635	No abnormalities detected	1-19, 51-65
	Eye discolored, Pale, Eye/left	66
	Eye discolored, Pale, Eye/right	66
	Hair sparse, Face	20-50
	Posture hunched	66
	Scabbed area, Face	23-26
	Scabbed area, Inguinal region/right	66
	Thin	66
1636	No abnormalities detected	1-5
	Hair sparse, Forelimb/left	14-76
	Hair sparse, Forelimb/right	14-76
	Nodule, 1-5 mm, Axillary region/left	48-62
	Salivation	6-13
	Swelling, Anogenital region	75, 76
	Swelling, Axillary region/right	56-62
	Swelling, Inguinal region/right	63-76
1637	No abnormalities detected	1-44
	Activity decreased	87
	Ear/portion of ear missing, Ear/left	51-87
	Nodule, 1-5 mm, Cervical region	78-87
	Posture hunched	87

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number		Week(s) Sign Present
<u>500 mg/kg/day</u>		
1637	Scabbed area, Ear/left	45-50
	Swelling, Axillary region/right	74-87
	Thin	87
1638	No abnormalities detected	1-3, 88-95
	Eye discolored, Pale, Eye/left	96
	Eye discolored, Pale, Eye/right	96
	Hair sparse, Cervical region	39-87
	Hair sparse, Face	4-87
	Hair sparse, Thoracic region	10-87
	Scabbed area, Face	23-27, 32-76
	Swelling, Inguinal region/left	52-62
1639	No abnormalities detected	1-13
	Hair sparse, Abdominal region	16-24
	Hair sparse, Forelimb/left	19-28
	Hair sparse, Forelimb/right	19-28
	Hair sparse, Thoracic region	14-28
	Hair sparse, Ventral surface	25-28
1640	No abnormalities detected	1-4, 8-13
	Hair sparse, Cervical region	19-87
	Hair sparse, Face	14-40
	Hair sparse, Forefoot/right	38-87

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Detailed Clinical Observations - FEMALE

Group, Animal Number		Week(s) Sign Present
<u>500 mg/kg/day</u>		
1640	Hair sparse, Shoulder/left	25-33
	Hair sparse, Shoulder/right	25-87
	Hair sparse, Thoracic region	16-33
	Hair sparse, Ventral surface	25-33
	Posture hunched	87
	Salivation	74-76
	Swelling, Anogenital region	83-87
	Thin	5-7, 87

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Unscheduled Detailed Clinical Observations - FEMALE

Group, Animal Number		Week(s) Sign Present
<u>0 mg/kg/day</u>		
1340	Activity decreased	99
	Material around eyes, Red, Eye/left	99
	Material around eyes, Red, Eye/right	99
	Posture hunched	99
	Swelling, Anogenital region	99
	Swelling, Axillary region/left	99
	Thin	99
1343	Activity decreased	65, 73
	Feces few/absent	65, 73
	Head tilt	73
	Material around eyes, Brown, Eye/left	73
	Material around eyes, Brown, Eye/right	73
	Piloerection	65, 73
	Righting reflex impaired	73
	Thin	73
1344	Thin	59
1347	Teeth cut	94
1354	Activity decreased	91

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Unscheduled Detailed Clinical Observations - FEMALE

Group, Animal Number	Week(s) Sign Present
<u>0 mg/kg/day</u>	
1354 Breathing shallow	91
Eyelid partially/completely closed, Eye/left	91
Eyelid partially/completely closed, Eye/right	91
Hair discolored, Yellow, Anogenital region	91
Posture hunched	91
1359 Activity decreased	73
Head tilt	73
Piloerection	73
Righting reflex lost	73
1365 Teeth cut	89
1371 Limb function impaired, Forelimb/left	48
Limb function impaired, Hind limb/left	21, 48
Swelling, Forelimb/left	48
Swelling, Hind foot/left	21, 48
1379 Hair discolored, Red, Face	62
Material around nose, Red	62
Piloerection	62
Posture hunched	62
Thin	62

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Unscheduled Detailed Clinical Observations - FEMALE

Group, Animal Number	Week(s) Sign Present
<u>0 mg/kg/day</u>	
1385 No abnormalities detected	88
1386 Activity decreased	88
Limb function impaired, Forelimb/right	88
Material around nose, Red	88
1388 Activity decreased	65
Righting reflex impaired	65
1393 Hair sparse, Forefoot/left	88
Hair sparse, Forefoot/right	88
Malocclusion	88
Teeth broken	88
Teeth cut	88
1399 Hair sparse, Cervical region	50, 51
Laceration, Abdominal region	51
Laceration, Hind limb/left	51
Limb function impaired, Hind limb/left	50
Limb function impaired, Hind limb/right	50, 51
Limb function lost, Hind limb/left	51

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Unscheduled Detailed Clinical Observations - FEMALE

Group, Animal Number	Week(s) Sign Present
<u>1 mg/kg/day</u>	
1424 No abnormalities detected	64
1426 Activity decreased	83
Breathing audible	83
Piloerection	83
1433 Head tilt	78
1436 Activity decreased	89, 90
Breathing audible	90
Breathing shallow	89, 90
Carriage low	89
Eyelid partially/completely closed, Eye/left	89, 90
Eyelid partially/completely closed, Eye/right	90
Hair discolored, Yellow, Ventral surface	89, 90
Piloerection	89, 90
Posture hunched	90
1441 Activity decreased	75
Breathing audible	75

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Unscheduled Detailed Clinical Observations - FEMALE

Group, Animal Number		Week(s) Sign Present
<u>1 mg/kg/day</u>		
1441	Breathing shallow	75
	Breathing slow	75
	Head tilt	75
	Hypersensitive to touch	75
	Material around eyes, Brown, Eye/left	75
	Material around eyes, Brown, Eye/right	75
	Righting reflex lost	75
1457	Activity decreased	82
	Ataxia	82
	Carriage low	82
	Inappetence	82
1462	Activity decreased	59
	Breathing audible	59
	Breathing difficult	59
	Material around nose, Red	59
1468	Activity decreased	79
	Breathing audible	79
	Breathing difficult	79
	Material around eyes, Black, Eye/right	79

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Unscheduled Detailed Clinical Observations - FEMALE

Group, Animal Number		Week(s) Sign Present
<u>1 mg/kg/day</u>		
1468	Material around nose, Black	79
	Piloerection	79
	Posture hunched	79
	Righting reflex impaired	79
	Thin	79
	Unkempt appearance	79
1474	Head tilt	52
	Leaning	52
	Posture hunched	52
	Righting reflex impaired	52
1475	Head tilt	101
	Piloerection	101
	Thin	101
1480	Activity decreased	78
	Leaning	78
	Righting reflex impaired	78

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Unscheduled Detailed Clinical Observations - FEMALE

Group, Animal Number		Week(s) Sign Present
<u>50 mg/kg/day</u>		
1494	Activity decreased	101
	Hair wet, Anogenital region	101
	Righting reflex impaired	101
1497	Head tilt	57
	Material around nose, Red	57
	Righting reflex impaired	57
1498	Head tilt	55
	Thin	55
1505	Eye protruding, Eye/left	85
	Head tilt	85
1507	Activity decreased	61
	Breathing slow	61
	Material around eyes, Red, Eye/left	61
	Material around eyes, Red, Eye/right	61
	Piloerection	61
	Prostration	61
	Righting reflex impaired	61
1513	Limb function impaired, Hind limb/left	41

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Unscheduled Detailed Clinical Observations - FEMALE

Group, Animal Number	Week(s) Sign Present
<u>50 mg/kg/day</u>	
1518 Activity decreased	25
Posture hunched	25
Skin cold to touch, Entire body	25
1525 Righting reflex impaired	75
1529 Breathing difficult	64
Moribund	64
1536 Ataxia	56
Breathing shallow	56
Hair sparse, Cervical region	56
Head tilt	56
Material around nose, Brown	56
Piloerection	56
Posture hunched	56
Righting reflex impaired	56
1552 Head tilt	52
Material around nose, Red	52
1554 Activity decreased	70

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Unscheduled Detailed Clinical Observations - FEMALE

Group, Animal Number		Week(s) Sign Present
<u>50 mg/kg/day</u>		
1554	Breathing shallow	70
	Head tilt	70
	Righting reflex lost	70
1557	Activity decreased	95
	Feces few/absent	95
	Hair discolored, Yellow, Anogenital region	95
	Inappetence	95
	Material around eyes, Red, Eye/left	95
	Material around eyes, Red, Eye/right	95
	Material around mouth, Red	95
	Piloerection	95
	Posture hunched	95
	Teeth chattering	95
<u>500 mg/kg/day</u>		
1580	Activity decreased	51
	Ataxia	51
	Head tilt	51
	Material around nose, Red	51
1583 ^r	Scabbed area, Thoracic region	57

^r Replacement animal

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Unscheduled Detailed Clinical Observations - FEMALE

Group, Animal Number		Week(s) Sign Present
<u>500 mg/kg/day</u>		
1598	Hair discolored, Brown, Ventral surface	76
	Hair wet, Ventral surface	76
	Salivation	76
	Unkempt appearance	76
1602	Activity decreased	85
	Breathing shallow	85
	Carriage low	85
	Eyelid partially/completely closed, Eye/left	85
	Eyelid partially/completely closed, Eye/right	85
	Feces few/absent	85
	Piloerection	85
	Posture hunched	85
	Unkempt appearance	85
1609	Activity decreased	99
	Lacrimation, Eye/left	99
	Lacrimation, Eye/right	99
	Material around nose, Red	99
	Skin cold to touch, Entire body	99
1610	Activity decreased	45
	Material around nose, Red	45

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Unscheduled Detailed Clinical Observations - FEMALE

Group, Animal Number		Week(s) Sign Present
<u>500 mg/kg/day</u>		
1610	Posture hunched	45
	Skin cold to touch, Entire body	45
	Thin	45
1627	Scabbed area, Axillary region/right	57
1640	Material around eyes, Red, Eye/left	42
	Material around eyes, Red, Eye/right	42
	Material around nose, Red	42
	Posture hunched	42
	Thin	42

Appendix E
Individual Mass Findings

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - MALE

Group, Animal Number		Week(s) Sign Present
<u>0 mg/kg/day</u>		
1001	No Masses Detected	1-52
1002	No Masses Detected	1-52
1003	No Masses Detected	1-52
1004	No Masses Detected	1-52
1005	No Masses Detected	1-52
1006	No Masses Detected	1-52
1007	No Masses Detected	1-52
1008	No Masses Detected	1-52
1009	No Masses Detected	1-52
1010	No Masses Detected	1-52
1011	No Masses Detected	1-103
1012	No Masses Detected	1-90
1013	No Masses Detected	1-94

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - MALE

Group, Animal Number		Week(s) Sign Present
<u>0 mg/kg/day</u>		
1014	No Masses Detected	1-103
1015	No Masses Detected	1-103
1016	No Masses Detected	1-70
	Mass 1, Thoracic region, Large ≥ 4 cm	76-86
	Mass 1, Thoracic region, Medium 2-3.9 cm	71-75
1017	No Masses Detected	1-69
1018	No Masses Detected	1-93
1019	No Masses Detected	1-71
	Mass 1, Axillary region/right, Medium 2-3.9 cm	75-78
	Mass 1, Axillary region/right, Small 1-1.9 cm	72-74
1020	No Masses Detected	1-77
1021	No Masses Detected	1-98
1022	No Masses Detected	1-99
1023	No Masses Detected	1-87
1024	No Masses Detected	1-92

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - MALE

Group, Animal Number		Week(s) Sign Present
<u>0 mg/kg/day</u>		
1025	No Masses Detected	1-103
1026	No Masses Detected	1-103
1027	No Masses Detected	1-62
1028	No Masses Detected	1-91
1029	No Masses Detected	1-103
1030	No Masses Detected	1-85
1031	No Masses Detected	1-103
1032	No Masses Detected	1-65
1033	No Masses Detected	1-42
1034	No Masses Detected	1-63
1035	No Masses Detected	1-103
1036	No Masses Detected	1-103
1037	No Masses Detected	1-89

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - MALE

Group, Animal Number		Week(s) Sign Present
<u>0 mg/kg/day</u>		
1038	No Masses Detected	1-67
1039	No Masses Detected	1-101
1040	No Masses Detected	1-94
1041	No Masses Detected	1-103
1042	No Masses Detected	1-89
1043	No Masses Detected	1-76
1044	No Masses Detected	1-43
1045	No Masses Detected	1-103
1046	No Masses Detected	1-27
1047	No Masses Detected	1-68
1048	No Masses Detected	1-54
1049	No Masses Detected	1-70
	Mass 1, Axillary region/right, Medium 2-3.9 cm	75-85
	Mass 1, Axillary region/right, Small 1-1.9 cm	71-74

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - MALE

Group, Animal Number		Week(s) Sign Present
<u>0 mg/kg/day</u>		
1050	No Masses Detected	1-85
1051	No Masses Detected	1-91
1052	No Masses Detected	1-43
	Mass 1, Axillary region/right, Large ≥ 4 cm	63-88
	Mass 1, Axillary region/right, Medium 2-3.9 cm	47-62
	Mass 1, Axillary region/right, Small 1-1.9 cm	44-46
1053	No Masses Detected	1-64
1054	No Masses Detected	1-98
1055	No Masses Detected	1-86
1056	No Masses Detected	1-57
1057	No Masses Detected	1-96
1058	No Masses Detected	1-71
	Mass 1, Axillary region/right, Medium 2-3.9 cm	74-81
	Mass 1, Axillary region/right, Small 1-1.9 cm	72, 73
1059	No Masses Detected	1-27
1060	No Masses Detected	1-99

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - MALE

Group, Animal Number		Week(s) Sign Present
<u>0 mg/kg/day</u>		
1061	No Masses Detected	1-71
1062	No Masses Detected	1-103
1063 ^{1,r}	No Masses Detected	3-98
1064	No Masses Detected	1-71
1065	No Masses Detected	1-82
1066	No Masses Detected	1-67
1067	No Masses Detected	1-103
1068	No Masses Detected	1-103
1069	No Masses Detected	1-77
1070	No Masses Detected	1-75
1071	No Masses Detected	1-101
1072	No Masses Detected	1-98
1073	No Masses Detected	1-95

¹ No observation for Week(s) 1-2

^r Replacement animal

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - MALE

Group, Animal Number		Week(s) Sign Present
<u>0 mg/kg/day</u>		
1074	No Masses Detected	1-55
1075	No Masses Detected	1-103
1076	No Masses Detected	1-103
1077	No Masses Detected	1-103
1078	No Masses Detected	1-71
	Mass 1, Axillary region/left, Large ≥ 4 cm	74-85
	Mass 1, Axillary region/left, Mass > 10cm	86, 87
	Mass 1, Axillary region/left, Medium 2-3.9 cm	72, 73
	Mass 1, Axillary region/left, Ulcerated, large ≥ 4 cm	88
1079	No Masses Detected	1-88
1080	No Masses Detected	1-98
<u>0.1 mg/kg/day</u>		
1081	No Masses Detected	1-52
1082	No Masses Detected	1-52
1083	No Masses Detected	1-52
1084	No Masses Detected	1-52

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - MALE

Group, Animal Number		Week(s) Sign Present
<u>0.1 mg/kg/day</u>		
1085	No Masses Detected	1-52
1086	No Masses Detected	1-52
1087	No Masses Detected	1-52
1088	No Masses Detected	1-52
1089	No Masses Detected	1-52
1090	No Masses Detected	1-52
1091	No Masses Detected	1-103
1092	No Masses Detected	1-58
1093	No Masses Detected	1-103
1094	No Masses Detected	1-103
1095	No Masses Detected	1-72
1096	No Masses Detected	1-103
1097	No Masses Detected	1-103

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - MALE

Group, Animal Number		Week(s) Sign Present
<u>0.1 mg/kg/day</u>		
1098	No Masses Detected	1-91
1099	No Masses Detected	1-103
1100	No Masses Detected	1-94
1101	No Masses Detected	1-55
1102	No Masses Detected	1-92
1103	No Masses Detected	1-19
1104	No Masses Detected	1-62
1105	No Masses Detected	1-93
1106	No Masses Detected	1-41
1107	No Masses Detected	1-103
1108	No Masses Detected	1-89
1109	No Masses Detected	1-103
1110	No Masses Detected	1-95

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - MALE

Group, Animal Number		Week(s) Sign Present
<u>0.1 mg/kg/day</u>		
1110	Mass 1, Inguinal region/left, Medium 2-3.9 cm	97, 98
	Mass 1, Inguinal region/left, Small 1-1.9 cm	96
1111	No Masses Detected	1-46
1112	No Masses Detected	1-103
1113	No Masses Detected	1-84
	Mass 1, Dorsal surface, Large ≥ 4 cm	88
	Mass 1, Dorsal surface, Mass > 10 cm	89
	Mass 1, Dorsal surface, Medium 2-3.9 cm	85-87
1114	No Masses Detected	1-72
1115	No Masses Detected	1-85
	Mass 1, Cervical region, Large ≥ 4 cm	89-92
	Mass 1, Cervical region, Medium 2-3.9 cm	86-88
1116	No Masses Detected	1-3
1117	No Masses Detected	1-89
1118	No Masses Detected	1-84
1119	No Masses Detected	1-50

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - MALE

Group, Animal Number		Week(s) Sign Present
<u>0.1 mg/kg/day</u>		
1120	No Masses Detected	1-103
1121	No Masses Detected	1-84
1122	No Masses Detected	1-103
1123	No Masses Detected	1-103
1124	No Masses Detected	1-103
1125	No Masses Detected	1-100
1126	No Masses Detected	1-98
1127	No Masses Detected	1-103
1128	No Masses Detected	1-79
1129	No Masses Detected	1-85
1130	No Masses Detected	1-101
1131	No Masses Detected	1-64
1132	No Masses Detected	1-103

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - MALE

Group, Animal Number		Week(s) Sign Present
<u>0.1 mg/kg/day</u>		
1133	No Masses Detected	1-90
1134	No Masses Detected	1-101
1135	No Masses Detected	1-94
1136	No Masses Detected	1-92
1137	No Masses Detected	1-76
1138	No Masses Detected	1-87
	Mass 1, Cervical region, Large ≥ 4 cm	96-99
	Mass 1, Cervical region, Medium 2-3.9 cm	92-95
	Mass 1, Cervical region, Small 1-1.9 cm	88-91
1139	No Masses Detected	1-12
1140	No Masses Detected	1-103
1141	No Masses Detected	1-58
1142	No Masses Detected	1-55
1143	No Masses Detected	1-103
1144	No Masses Detected	1-47

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - MALE

Group, Animal Number		Week(s) Sign Present
<u>0.1 mg/kg/day</u>		
1145	No Masses Detected	1-47
1146	No Masses Detected	1-75
1147	No Masses Detected	1-103
1148	No Masses Detected	1-81
1149	No Masses Detected	1-74
	Mass 1, Anogenital region, Large ≥ 4 cm	80-88
	Mass 1, Anogenital region, Medium 2-3.9 cm	75-79
1150	No Masses Detected	1-103
1151	No Masses Detected	1-83
1152	No Masses Detected	1-73
1153	No Masses Detected	1-89
1154	No Masses Detected	1-103
1155	No Masses Detected	1-35
1156	No Masses Detected	1-77

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - MALE

Group, Animal Number		Week(s) Sign Present
<u>0.1 mg/kg/day</u>		
1156	Mass 1, Cervical region, Medium 2-3.9 cm	80, 81
	Mass 1, Cervical region, Small 1-1.9 cm	78, 79
1157	No Masses Detected	1-101
1158	No Masses Detected	1-89
1159	No Masses Detected	1-101
1160	No Masses Detected	1-92
<u>1 mg/kg/day</u>		
1161	No Masses Detected	1-52
1162	No Masses Detected	1-52
1163	No Masses Detected	1-52
1164	No Masses Detected	1-52
1165	No Masses Detected	1-52
1166	No Masses Detected	1-52
1167	No Masses Detected	1-52

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - MALE

Group, Animal Number		Week(s) Sign Present
<u>1 mg/kg/day</u>		
1168	No Masses Detected	1-52
1169	No Masses Detected	1-52
1170	No Masses Detected	1-52
1171	No Masses Detected	1-103
1172	No Masses Detected	1-81
1173	No Masses Detected	1-72
	Mass 1, Thoracic region, Small 1-1.9 cm	73-79
1174	No Masses Detected	1-43
1175	No Masses Detected	1-90
1176	No Masses Detected	1-103
1177	No Masses Detected	1-43
1178	No Masses Detected	1-99
	Mass 1, Inguinal region/right, Medium 2-3.9 cm	103
	Mass 1, Inguinal region/right, Small 1-1.9 cm	100-102
1179	No Masses Detected	1-73

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - MALE

Group, Animal Number		Week(s) Sign Present
<u>1 mg/kg/day</u>		
1180	No Masses Detected	1-103
1181	No Masses Detected	1-57
1182	No Masses Detected	1-64
1183	No Masses Detected	1-76
1184	No Masses Detected	1-84
1185	No Masses Detected	1-78
1186	No Masses Detected	1-103
1187	No Masses Detected	1-78
1188	No Masses Detected Mass 1, Dorsal surface, Large >or=4 cm	1-79 80-86
1189	No Masses Detected	1-65
1190	No Masses Detected	1-35
1191	No Masses Detected	1-51
1192	No Masses Detected	1-103

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - MALE

Group, Animal Number		Week(s) Sign Present
<u>1 mg/kg/day</u>		
1193	No Masses Detected	1-96
	Mass 1, Axillary region/right, Medium 2-3.9 cm	103
	Mass 1, Axillary region/right, Small 1-1.9 cm	97-102
1194	No Masses Detected	1-103
1195	No Masses Detected	1-86
1196	No Masses Detected	1-93
1197	No Masses Detected	1-66
1198	No Masses Detected	1-89
1199	No Masses Detected	1-103
1200	No Masses Detected	1-96
1201	No Masses Detected	1-77
1202	No Masses Detected	1-103
1203	No Masses Detected	1-43
1204	No Masses Detected	1-103

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - MALE

Group, Animal Number		Week(s) Sign Present
<u>1 mg/kg/day</u>		
1205	No Masses Detected	1-73
	Mass 1, Cervical region, Medium 2-3.9 cm	75, 76
	Mass 1, Cervical region, Small 1-1.9 cm	74
1206	No Masses Detected	1-78
1207	No Masses Detected	1-29
1208	No Masses Detected	1-72
1209	No Masses Detected	1-88
1210	No Masses Detected	1-97
	Mass 1, Thoracic region, BI Medium Ulcerated 2-4cm	98
1211	No Masses Detected	1-103
1212	No Masses Detected	1-103
1213	No Masses Detected	1-89
1214	No Masses Detected	1-68
1215	No Masses Detected	1-70
1216	No Masses Detected	1-56

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - MALE

Group, Animal Number		Week(s) Sign Present
<u>1 mg/kg/day</u>		
1217	No Masses Detected	1-100
1218	No Masses Detected	1-103
1219	No Masses Detected	1-79
1220	No Masses Detected	1-97
1221	No Masses Detected	1-103
1222	No Masses Detected	1-68
1223	No Masses Detected	1-95
	Mass 1, Thoracic region, Large ≥ 4 cm	100-103
	Mass 1, Thoracic region, Medium 2-3.9 cm	98, 99
	Mass 1, Thoracic region, Small 1-1.9 cm	96, 97
1224	No Masses Detected	1-64
	Mass 1, Cranial region, Medium 2-3.9 cm	66, 67
	Mass 1, Cranial region, Small 1-1.9 cm	65
1225	No Masses Detected	1-99
	Mass 1, Thoracic region, Medium 2-3.9 cm	103
	Mass 1, Thoracic region, Small 1-1.9 cm	100-102
1226	No Masses Detected	1-76

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - MALE

Group, Animal Number		Week(s) Sign Present
<u>1 mg/kg/day</u>		
1227	No Masses Detected	1-103
1228	No Masses Detected	1-57
1229	No Masses Detected	1-94
1230	No Masses Detected	1-37
1231	No Masses Detected	1-60
1232	No Masses Detected	1-81
1233	No Masses Detected	1-59
1234	No Masses Detected	1-58
1235	No Masses Detected	1-64
1236	No Masses Detected	1-102
1237	No Masses Detected	1-50
1238	No Masses Detected	1-67
1239	No Masses Detected	1-88

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - MALE

Group, Animal Number		Week(s) Sign Present
<u>1 mg/kg/day</u>		
1240	No Masses Detected	1-103
<u>50 mg/kg/day</u>		
1241	No Masses Detected	1-52
1242	No Masses Detected	1-52
1243	No Masses Detected	1-52
1244	No Masses Detected	1-52
1245	No Masses Detected	1-52
1246	No Masses Detected	1-52
1247	No Masses Detected	1-52
1248	No Masses Detected	1-52
1249 ^r	No Masses Detected	1-52
1250	No Masses Detected	1-52
1251	No Masses Detected	1-103
1252	No Masses Detected	1-103

^r Replacement animal

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - MALE

Group, Animal Number		Week(s) Sign Present
<u>50 mg/kg/day</u>		
1253	No Masses Detected	1-87
1254	No Masses Detected	1-103
1255	No Masses Detected	1-103
1256	No Masses Detected	1-65
1257	No Masses Detected	1-103
1258	No Masses Detected	1-96
1259	No Masses Detected	1-65
1260	No Masses Detected	1-102
1261	No Masses Detected	1-103
1262	No Masses Detected	1-82
1263	No Masses Detected	1-86
1264	No Masses Detected	1-79
1265	No Masses Detected	1-72

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - MALE

Group, Animal Number		Week(s) Sign Present
<u>50 mg/kg/day</u>		
1266	No Masses Detected	1-83
1267	No Masses Detected	1-89
1268	No Masses Detected	1-56
1269	No Masses Detected	1-92
1270	No Masses Detected	1-94
	Mass 1, Axillary region/right, Medium 2-3.9 cm	100-103
	Mass 1, Axillary region/right, Small 1-1.9 cm	95-99
1271	No Masses Detected	1-103
1272	No Masses Detected	1-49
1273	No Masses Detected	1-54
1274	No Masses Detected	1-83
1275	No Masses Detected	1-77
1276	No Masses Detected	1-85
1277	No Masses Detected	1-103

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - MALE

Group, Animal Number		Week(s) Sign Present
<u>50 mg/kg/day</u>		
1278	No Masses Detected	1-87
1279	No Masses Detected	1-70
1280	No Masses Detected	1-103
1281	No Masses Detected	1-59
1282	No Masses Detected	1-73
	Mass 1, Axillary region/right, Large ≥ 4 cm	85-95
	Mass 1, Axillary region/right, Medium 2-3.9 cm	74-84
1283	No Masses Detected	1-99
	Mass 1, Inguinal region/right, Small 1-1.9 cm	100-103
1284	No Masses Detected	1-50
1285	No Masses Detected	1-61
1286	No Masses Detected	1-103
1287	No Masses Detected	1-103
1288	No Masses Detected	1-81, 85
	Mass 1, Abdominal region, Large ≥ 4 cm	83, 84, 86-88

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - MALE

Group, Animal Number		Week(s) Sign Present
<u>50 mg/kg/day</u>		
1288	Mass 1, Abdominal region, Medium 2-3.9 cm	82
1289	No Masses Detected	1-103
1290	No Masses Detected	1-81
1291	No Masses Detected	1-102
1292	No Masses Detected	1-63
1293	No Masses Detected	1-88
1294	No Masses Detected	1-103
1295	No Masses Detected	1-103
1296	No Masses Detected	1-42
	Mass 1, Axillary region/left, Large ≥ 4 cm	57
	Mass 1, Axillary region/left, Mass > 10 cm	58
	Mass 1, Axillary region/left, Medium 2-3.9 cm	50-56
	Mass 1, Axillary region/left, Small 1-1.9 cm	43-49
1297	No Masses Detected	1-103
1298	No Masses Detected	1-63

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - MALE

Group, Animal Number		Week(s) Sign Present
<u>50 mg/kg/day</u>		
1299	No Masses Detected	1-85
1300	No Masses Detected	1-57
1301	No Masses Detected	1-87
	Mass 1, Axillary region/left, Small 1-1.9 cm	88-90
1302	No Masses Detected	1-59
1303	No Masses Detected	1-87
1304	No Masses Detected	1-77
1305	No Masses Detected	1-79
1306	No Masses Detected	1-60
1307	No Masses Detected	1-91
1308	No Masses Detected	1-96
	Mass 1, Thoracic region, Large >or=4 cm	100, 101
	Mass 1, Thoracic region, Medium 2-3.9 cm	97-99
1309	No Masses Detected	1-103
1310	No Masses Detected	1-81

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - MALE

Group, Animal Number		Week(s) Sign Present
<u>50 mg/kg/day</u>		
1311	No Masses Detected	1-103
1312	No Masses Detected	1-45
1313	No Masses Detected	1-101
1314	No Masses Detected	1-91
	Mass 1, Hind limb/left, Large ≥ 4 cm	97, 98
	Mass 1, Hind limb/left, Mass > 10 cm	99, 100
	Mass 1, Hind limb/left, Medium 2-3.9 cm	96
	Mass 1, Hind limb/left, Small 1-1.9 cm	92-95
1315	No Masses Detected	1-103
1316	No Masses Detected	1-26
	Mass 1, Axillary region/right, Large ≥ 4 cm	43-58
	Mass 1, Axillary region/right, Medium 2-3.9 cm	29-42
	Mass 1, Axillary region/right, Small 1-1.9 cm	27, 28
1317	No Masses Detected	1-56
1318	No Masses Detected	1-53
1319	No Masses Detected	1-103
1320	No Masses Detected	1-62

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - FEMALE

Group, Animal Number		Week(s) Sign Present
<u>0 mg/kg/day</u>		
1321	No Masses Detected	1-49
1322	No Masses Detected	1-52
1323	No Masses Detected	1-44
1324	No Masses Detected	1-52
1325	No Masses Detected	1-52
1326	No Masses Detected	1-52
1327	No Masses Detected	1-52
1328	No Masses Detected	1-52
1329	No Masses Detected	1-52
1330	No Masses Detected	1-52
1331	No Masses Detected	1-52
1332	No Masses Detected	1-52
1333	No Masses Detected	1-100

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - FEMALE

Group, Animal Number		Week(s) Sign Present
<u>0 mg/kg/day</u>		
1334	No Masses Detected	1-83
	Mass 1, Axillary region/left, Medium 2-3.9 cm	86-95
	Mass 1, Axillary region/left, Small 1-1.9 cm	84, 85
	Mass 2, Axillary region/left, Small 1-1.9 cm	89-95
	Mass 3, Inguinal region/left, Medium 2-3.9 cm	89-95
	Mass 4, Inguinal region/right, Small 1-1.9 cm	89-95
	Mass 5, Axillary region/right, Small 1-1.9 cm	95
1335	No Masses Detected	1-64
	Mass 1, Anogenital region, Large ≥ 4 cm	96-100
	Mass 1, Anogenital region, Medium 2-3.9 cm	72-95
	Mass 1, Anogenital region, Small 1-1.9 cm	65-71
	Mass 2, Inguinal region/left, Medium 2-3.9 cm	97-100
	Mass 2, Inguinal region/left, Small 1-1.9 cm	89-96
1336	No Masses Detected	1-60
	Mass 1, Anogenital region, Medium 2-3.9 cm	63-93
	Mass 1, Anogenital region, Small 1-1.9 cm	61, 62
	Mass 2, Axillary region/left, Medium 2-3.9 cm	89-93
	Mass 2, Axillary region/left, Small 1-1.9 cm	75-88
	Mass 3, Inguinal region/left, Small 1-1.9 cm	83-93
1337	No Masses Detected	1-14
	Mass 1, Thoracic region, Large ≥ 4 cm	39-54
	Mass 1, Thoracic region, Medium 2-3.9 cm	18-38

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - FEMALE

Group, Animal Number		Week(s) Sign Present
<u>0 mg/kg/day</u>		
1337	Mass 1, Thoracic region, Small 1-1.9 cm	15-17
1338	No Masses Detected	1-81
	Mass 1, Axillary region/left, Small 1-1.9 cm	82-87
	Mass 2, Axillary region/right, Ulcerated, small 1-1.9 cm	87
1339	No Masses Detected	1-64
	Mass 1, Anogenital region, Medium 2-3.9 cm	74-100
	Mass 1, Anogenital region, Small 1-1.9 cm	65-73
	Mass 2, Axillary region/right, Small 1-1.9 cm	89-100
1340	No Masses Detected	1-88
	Mass 1, Anogenital region, Medium 2-3.9 cm	90-98
	Mass 1, Anogenital region, Small 1-1.9 cm	89
1341	No Masses Detected	1-28
	Mass 1, Axillary region/right, Medium 2-3.9 cm	33-35
	Mass 1, Axillary region/right, Small 1-1.9 cm	29-32
	Mass 1, Axillary region/right, Ulcerated, medium 2-3.9 cm	36
1342	No Masses Detected	1-46
	Mass 1, Axillary region/right, Large ≥ 4 cm	63-67
	Mass 1, Axillary region/right, Mass > 10 cm	68
	Mass 1, Axillary region/right, Medium 2-3.9 cm	61, 62
	Mass 1, Axillary region/right, Small 1-1.9 cm	47-60

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - FEMALE

Group, Animal Number		Week(s) Sign Present
<u>0 mg/kg/day</u>		
1343	No Masses Detected	1-72
1344	No Masses Detected	1-46
	Mass 1, Thoracic region, Large ≥ 4 cm	56-59
	Mass 1, Thoracic region, Small 1-1.9 cm	47-55
1345	No Masses Detected	1-85
1346	No Masses Detected	1-37
	Mass 1, Thoracic region, Large ≥ 4 cm	56, 57
	Mass 1, Thoracic region, Mass > 10 cm	58
	Mass 1, Thoracic region, Medium 2-3.9 cm	47-55
	Mass 1, Thoracic region, Small 1-1.9 cm	38-46
1347	No Masses Detected	1-100
1348	No Masses Detected	1-87
1349	No Masses Detected	1-66
1350	No Masses Detected	1-66
1351	No Masses Detected	1-60
	Mass 1, Axillary region/left, Large ≥ 4 cm	68-70
	Mass 1, Axillary region/left, Medium 2-3.9 cm	65-67

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - FEMALE

Group, Animal Number		Week(s) Sign Present
<u>0 mg/kg/day</u>		
1351	Mass 1, Axillary region/left, Small 1-1.9 cm	61-64
	Mass 2, Axillary region/right, Medium 2-3.9 cm	68-70
	Mass 2, Axillary region/right, Small 1-1.9 cm	61-67
1352	No Masses Detected	1-88
	Mass 1, Cervical region, Medium 2-3.9 cm	97-100
	Mass 1, Cervical region, Small 1-1.9 cm	89-96
1353	No Masses Detected	1-88
	Mass 1, Inguinal region/right, Medium 2-3.9 cm	99, 100
	Mass 1, Inguinal region/right, Small 1-1.9 cm	89-98
	Mass 2, Inguinal region/right, Medium 2-3.9 cm	99, 100
	Mass 2, Inguinal region/right, Small 1-1.9 cm	89-98
1354	No Masses Detected	1-90
1355	No Masses Detected	1-100
1356	No Masses Detected	1-64
	Mass 1, Axillary region/left, Small 1-1.9 cm	65, 66
	Mass 2, Inguinal region/left, Small 1-1.9 cm	65, 66
1357	No Masses Detected	1-100
1358	No Masses Detected	1-88

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - FEMALE

Group, Animal Number		Week(s) Sign Present
<u>0 mg/kg/day</u>		
1358	Mass 1, Thoracic region, Small 1-1.9 cm	89-100
1359	No Masses Detected	1-72
1360	No Masses Detected	1-74
	Mass 1, Inguinal region/left, Medium 2-3.9 cm	86-91
	Mass 1, Inguinal region/left, Small 1-1.9 cm	75-85
1361	No Masses Detected	1-82
	Mass 1, Inguinal region/left, Large ≥ 4 cm	90-93
	Mass 1, Inguinal region/left, Medium 2-3.9 cm	84-89
	Mass 1, Inguinal region/left, Small 1-1.9 cm	83
1362	No Masses Detected	1-74
	Mass 1, Anogenital region, Large ≥ 4 cm	90, 91
	Mass 1, Anogenital region, Medium 2-3.9 cm	79-89
	Mass 1, Anogenital region, Small 1-1.9 cm	75-78
	Mass 2, Thoracic region, Small 1-1.9 cm	89-91
1363	No Masses Detected	1-64
	Mass 1, Inguinal region/left, Large ≥ 4 cm	75-85
	Mass 1, Inguinal region/left, Mass > 10 cm	86
	Mass 1, Inguinal region/left, Medium 2-3.9 cm	71-74
	Mass 1, Inguinal region/left, Small 1-1.9 cm	65-70
1364	No Masses Detected	1-55

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - FEMALE

Group, Animal Number		Week(s) Sign Present
<u>0 mg/kg/day</u>		
1364	Mass 1, Inguinal region/left, Large ≥ 4 cm	67, 68
	Mass 1, Inguinal region/left, Medium 2-3.9 cm	56-66
	Mass 1, Inguinal region/left, Ulcerated, medium 2-3.9 cm	69
1365	No Masses Detected	1-100
1366	No Masses Detected	1-66
	Mass 1, Cervical region, Large ≥ 4 cm	79-91
	Mass 1, Cervical region, Medium 2-3.9 cm	71-78
	Mass 1, Cervical region, Small 1-1.9 cm	67-70
	Mass 2, Inguinal region/right, Medium 2-3.9 cm	90, 91
	Mass 2, Inguinal region/right, Small 1-1.9 cm	88, 89
1367	No Masses Detected	1-71
	Mass 1, Anogenital region, Large ≥ 4 cm	86-88
	Mass 1, Anogenital region, Medium 2-3.9 cm	79-85
	Mass 1, Anogenital region, Small 1-1.9 cm	72-78
1368	No Masses Detected	1-67
	Mass 1, Inguinal region/right, Large ≥ 4 cm	90-100
	Mass 1, Inguinal region/right, Medium 2-3.9 cm	72-89
	Mass 1, Inguinal region/right, Small 1-1.9 cm	68-71
1369	No Masses Detected	1-85
	Mass 1, Inguinal region/right, Small 1-1.9 cm	86

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - FEMALE

Group, Animal Number		Week(s) Sign Present
<u>0 mg/kg/day</u>		
1369	Mass 1, Inguinal region/right, Ulcerated, small 1-1.9 cm	87
1370	No Masses Detected	1-100
1371	No Masses Detected	1-47
1372	No Masses Detected	1-67
	Mass 1, Cervical region, Medium 2-3.9 cm	87-100
	Mass 1, Cervical region, Small 1-1.9 cm	68-86
1373	No Masses Detected	1-34
	Mass 1, Anogenital region, Small 1-1.9 cm	35-51
	Mass 2, Axillary region/right, Medium 2-3.9 cm	47-51
	Mass 2, Axillary region/right, Small 1-1.9 cm	37-46
1374	No Masses Detected	1-95
	Mass 1, Inguinal region/left, Medium 2-3.9 cm	99
	Mass 1, Inguinal region/left, Small 1-1.9 cm	96-98, 100
1375	No Masses Detected	1-64
	Mass 1, Anogenital region, Small 1-1.9 cm	65, 66
1376	No Masses Detected	1-62
	Mass 1, Anogenital region, Large ≥ 4 cm	72-85
	Mass 1, Anogenital region, Mass > 10 cm	86

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - FEMALE

Group, Animal Number		Week(s) Sign Present
<u>0 mg/kg/day</u>		
1376	Mass 1, Anogenital region, Medium 2-3.9 cm	67-71
	Mass 1, Anogenital region, Small 1-1.9 cm	63-66
	Mass 1, Anogenital region, Ulcerated, large ≥ 4 cm	87
1377	No Masses Detected	1-56
1378	No Masses Detected	1-73
1379	No Masses Detected	1-65
1380	No Masses Detected	1-35
	Mass 1, Inguinal region/left, Medium 2-3.9 cm	39-51
	Mass 1, Inguinal region/left, Small 1-1.9 cm	36-38
	Mass 1, Inguinal region/left, Ulcerated, large ≥ 4 cm	52
1381	No Masses Detected	1-66
1382	No Masses Detected	1-79
1383	No Masses Detected	1-60
	Mass 1, Axillary region/right, Large ≥ 4 cm	71-78
	Mass 1, Axillary region/right, Medium 2-3.9 cm	63-70
	Mass 1, Axillary region/right, Small 1-1.9 cm	61, 62
1384	No Masses Detected	1-69

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - FEMALE

Group, Animal Number		Week(s) Sign Present
<u>0 mg/kg/day</u>		
1384	Mass 1, Inguinal region/left, Small 1-1.9 cm	70-91
	Mass 2, Inguinal region/right, Small 1-1.9 cm	84-91
	Mass 3, Axillary region/right, Small 1-1.9 cm	84-91
	Mass 4, Axillary region/left, Small 1-1.9 cm	84-91
	Mass 5, Axillary region/left, Small 1-1.9 cm	89-91
	Mass 6, Axillary region/right, Small 1-1.9 cm	89-91
1385	No Masses Detected	1-71
	Mass 1, Axillary region/right, Medium 2-3.9 cm	81-93
	Mass 1, Axillary region/right, Small 1-1.9 cm	72-80
	Mass 1, Axillary region/right, Ulcerated, medium 2-3.9 cm	94
1386	No Masses Detected	1-88
1387	No Masses Detected	1-76
1388	No Masses Detected	1-64
1389	No Masses Detected	1-94
	Mass 1, Inguinal region/left, Medium 2-3.9 cm	99, 100
	Mass 1, Inguinal region/left, Small 1-1.9 cm	95-98
1390	No Masses Detected	1-62
	Mass 1, Inguinal region/left, Medium 2-3.9 cm	75-87
	Mass 1, Inguinal region/left, Small 1-1.9 cm	63-74

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - FEMALE

Group, Animal Number		Week(s) Sign Present
<u>0 mg/kg/day</u>		
1390	Mass 2, Axillary region/right, Small 1-1.9 cm	72-87
	Mass 3, Cervical region, Small 1-1.9 cm	82-87
1391	No Masses Detected	1-97
1392	No Masses Detected	1-100
1393	No Masses Detected	1-74
	Mass 1, Anogenital region, Medium 2-3.9 cm	84-88
	Mass 1, Anogenital region, Small 1-1.9 cm	75-83
	Mass 2, Face, Ulcerated, small 1-1.9 cm	88
1394	No Masses Detected	1-83
	Mass 1, Cervical region, Small 1-1.9 cm	84-96
	Mass 2, Axillary region/right, Small 1-1.9 cm	89-96
1395	No Masses Detected	1-61
1396	No Masses Detected	1-69
1397	No Masses Detected	1-100
1398	No Masses Detected	1-72
	Mass 1, Axillary region/left, Medium 2-3.9 cm	89-94
	Mass 1, Axillary region/left, Small 1-1.9 cm	73-88

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - FEMALE

Group, Animal Number		Week(s) Sign Present
<u>0 mg/kg/day</u>		
1399	No Masses Detected	1-50
1400	No Masses Detected	1-81
	Mass 1, Cervical region, Small 1-1.9 cm	82-89
	Mass 2, Lumbar region, Medium 2-3.9 cm	89
	Mass 3, Inguinal region/left, Small 1-1.9 cm	89
<u>1 mg/kg/day</u>		
1401	No Masses Detected	1-52
1402	No Masses Detected	1-52
1403	No Masses Detected	1-52
1404	No Masses Detected	1-52
1405	No Masses Detected	1-42
	Mass 1, Thoracic region, Small 1-1.9 cm	43-52
1406	No Masses Detected	1-52
1407	No Masses Detected	1-52
1408	No Masses Detected	1-52
1409	No Masses Detected	1-52

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - FEMALE

Group, Animal Number		Week(s) Sign Present
<u>1 mg/kg/day</u>		
1410	No Masses Detected	1-52
1411	No Masses Detected	1-57
1412	No Masses Detected	1-74
	Mass 1, Anogenital region, Medium 2-3.9 cm	90-96
	Mass 1, Anogenital region, Small 1-1.9 cm	75-89
	Mass 1, Anogenital region, Ulcerated, medium 2-3.9 cm	97
	Mass 2, Inguinal region/right, Medium 2-3.9 cm	87-97
	Mass 3, Inguinal region/left, Medium 2-3.9 cm	95-97
1413	No Masses Detected	1-78
	Mass 1, Axillary region/left, Small 1-1.9 cm	79-86
	Mass 2, Axillary region/right, Small 1-1.9 cm	79-86
1414	No Masses Detected	1-94
1415	No Masses Detected	1-72
	Mass 1, Axillary region/right, Medium 2-3.9 cm	98
	Mass 1, Axillary region/right, Small 1-1.9 cm	73-97
1416	No Masses Detected	1-95
	Mass 1, Cervical region, Small 1-1.9 cm	96-100
1417	No Masses Detected	1-60

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - FEMALE

Group, Animal Number		Week(s) Sign Present
<u>1 mg/kg/day</u>		
1417	Mass 1, Inguinal region/left, Large ≥ 4 cm	72-89
	Mass 1, Inguinal region/left, Medium 2-3.9 cm	66-71
	Mass 1, Inguinal region/left, Small 1-1.9 cm	61-65
	Mass 2, Abdominal region, Small 1-1.9 cm	86-89
1418	No Masses Detected	1-99
	Mass 1, Axillary region/left, Small 1-1.9 cm	100
1419	No Masses Detected	1-88
	Mass 1, Inguinal region/left, Large ≥ 4 cm	90-100
	Mass 1, Inguinal region/left, Medium 2-3.9 cm	89
1420	No Masses Detected	1-62
1421	No Masses Detected	1-35
	Mass 1, Axillary region/right, Small 1-1.9 cm	36-42
	Mass 1, Axillary region/right, Ulcerated, small 1-1.9 cm	43
1422	No Masses Detected	1-77
1423	No Masses Detected	1-63
1424	No Masses Detected	1-100
1425	No Masses Detected	1-100

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - FEMALE

Group, Animal Number		Week(s) Sign Present
<u>1 mg/kg/day</u>		
1426	No Masses Detected	1-73
	Mass 1, Axillary region/left, Small 1-1.9 cm	74-82
	Mass 2, Anogenital region, Small 1-1.9 cm	78-82
1427	No Masses Detected	1-72
1428	No Masses Detected	1-81
1429	No Masses Detected	1-94
	Mass 1, Cervical region, Small 1-1.9 cm	95-100
	Mass 2, Anogenital region, Small 1-1.9 cm	96-100
	Mass 3, Inguinal region/left, Small 1-1.9 cm	100
1430	No Masses Detected	1-94
	Mass 1, Inguinal region/right, Medium 2-3.9 cm	100
	Mass 1, Inguinal region/right, Small 1-1.9 cm	95-99
1431	No Masses Detected	1-100
1432	No Masses Detected	1-95
	Mass 1, Anogenital region, Medium 2-3.9 cm	100
	Mass 1, Anogenital region, Small 1-1.9 cm	96-99
1433	No Masses Detected	1-77
1434	No Masses Detected	1-87

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - FEMALE

Group, Animal Number		Week(s) Sign Present
<u>1 mg/kg/day</u>		
1434	Mass 1, Inguinal region/left, Small 1-1.9 cm	88-100
	Mass 2, Inguinal region/right, Medium 2-3.9 cm	90-100
	Mass 2, Inguinal region/right, Small 1-1.9 cm	88, 89
	Mass 3, Axillary region/right, Small 1-1.9 cm	99, 100
	Mass 4, Thoracic region, Small 1-1.9 cm	99, 100
1435	No Masses Detected	1-52
	Mass 1, Inguinal region/left, Large >or=4 cm	64-89
	Mass 1, Inguinal region/left, Mass > 10cm	90-100
	Mass 1, Inguinal region/left, Medium 2-3.9 cm	53-63
	Mass 2, Axillary region/right, Medium 2-3.9 cm	90-100
	Mass 2, Axillary region/right, Small 1-1.9 cm	85-89
	Mass 3, Inguinal region/right, Medium 2-3.9 cm	90-100
	Mass 3, Inguinal region/right, Small 1-1.9 cm	85-89
	Mass 4, Axillary region/right, Small 1-1.9 cm	94-100
1436	No Masses Detected	1-89
1437	No Masses Detected	1-98
	Mass 1, Axillary region/right, Small 1-1.9 cm	99, 100
	Mass 2, Inguinal region/right, Small 1-1.9 cm	99, 100
	Mass 3, Anogenital region, Small 1-1.9 cm	99, 100
1438	No Masses Detected	1-100
1439	No Masses Detected	1-97

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - FEMALE

Group, Animal Number		Week(s) Sign Present
<u>1 mg/kg/day</u>		
1440	No Masses Detected	1-88
	Mass 1, Anogenital region, Large ≥ 4 cm	100
	Mass 1, Anogenital region, Medium 2-3.9 cm	90-99
	Mass 1, Anogenital region, Small 1-1.9 cm	89
1441	No Masses Detected	1-74
1442	No Masses Detected	1-51
	Mass 1, Inguinal region/right, Large ≥ 4 cm	64-84
	Mass 1, Inguinal region/right, Mass > 10 cm	85
	Mass 1, Inguinal region/right, Medium 2-3.9 cm	52-63
1443	No Masses Detected	1-64
	Mass 1, Axillary region/left, Large ≥ 4 cm	87, 88
	Mass 1, Axillary region/left, Medium 2-3.9 cm	72-86
	Mass 1, Axillary region/left, Small 1-1.9 cm	65-71
1444	No Masses Detected	1-77
1445	No Masses Detected	1-55
1446	No Masses Detected	1-68
1447	No Masses Detected	1-99
	Mass 1, Inguinal region/left, Small 1-1.9 cm	100

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - FEMALE

Group, Animal Number		Week(s) Sign Present
<u>1 mg/kg/day</u>		
1448	No Masses Detected	1-86
1449	No Masses Detected	1-45
	Mass 1, Axillary region/right, Large ≥ 4 cm	64-73
	Mass 1, Axillary region/right, Medium 2-3.9 cm	52-63
	Mass 1, Axillary region/right, Small 1-1.9 cm	46-51
	Mass 2, Axillary region/left, Small 1-1.9 cm	66-73
1450	No Masses Detected	1-100
1451	No Masses Detected	1-51, 58
	Mass 1, Axillary region/left, Small 1-1.9 cm	52-92
	Mass 2, Anogenital region, Large ≥ 4 cm	75-89
	Mass 2, Anogenital region, Mass > 10 cm	90, 91
	Mass 2, Anogenital region, Medium 2-3.9 cm	64-74
	Mass 2, Anogenital region, Small 1-1.9 cm	58-63
	Mass 2, Anogenital region, Ulcerated, medium 2-3.9 cm	92
1452	No Masses Detected	1-73
	Mass 1, Axillary region/right, Medium 2-3.9 cm	78-80
	Mass 1, Axillary region/right, Small 1-1.9 cm	74-77
	Mass 1, Axillary region/right, Ulcerated, medium 2-3.9 cm	81
1453	No Masses Detected	1-51
	Mass 1, Anogenital region, Medium 2-3.9 cm	59

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - FEMALE

Group, Animal Number		Week(s) Sign Present
<u>1 mg/kg/day</u>		
1453	Mass 1, Anogenital region, Small 1-1.9 cm	52-58
	Mass 1, Anogenital region, Ulcerated, medium 2-3.9 cm	60
1454	No Masses Detected	1-98
	Mass 1, Inguinal region/right, Small 1-1.9 cm	99, 100
1455	No Masses Detected	1-86
1456	No Masses Detected	1-57
	Mass 1, Cervical region, Large >or=4 cm	64-84
	Mass 1, Cervical region, Medium 2-3.9 cm	59-63
	Mass 1, Cervical region, Small 1-1.9 cm	58
1457	No Masses Detected	1-81
1458	No Masses Detected	1-39
1459	No Masses Detected	1-74
1460	No Masses Detected	1-85
	Mass 1, Axillary region/left, Small 1-1.9 cm	86-100
1461	No Masses Detected	1-62
	Mass 1, Axillary region/left, Medium 2-3.9 cm	67-73
	Mass 1, Axillary region/left, Small 1-1.9 cm	63-66

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - FEMALE

Group, Animal Number		Week(s) Sign Present
<u>1 mg/kg/day</u>		
1461	Mass 2, Inguinal region/left, Small 1-1.9 cm	66-73
	Mass 3, Inguinal region/right, Ulcerated, medium 2-3.9 cm	73
1462	No Masses Detected	1-58
1463	No Masses Detected	1-79
	Mass 1, Inguinal region/left, Large ≥ 4 cm	87, 88
	Mass 1, Inguinal region/left, Medium 2-3.9 cm	86
	Mass 1, Inguinal region/left, Small 1-1.9 cm	80-85
1464	No Masses Detected	1-73
	Mass 1, Axillary region/right, Small 1-1.9 cm	74-79
	Mass 2, Anogenital region, Small 1-1.9 cm	75-79
1465	No Masses Detected	1-78
1466	No Masses Detected	1-30
1467	No Masses Detected	1-79
	Mass 1, Inguinal region/right, Medium 2-3.9 cm	100
	Mass 1, Inguinal region/right, Small 1-1.9 cm	80-99
	Mass 2, Axillary region/left, Medium 2-3.9 cm	90-100
	Mass 2, Axillary region/left, Small 1-1.9 cm	82-89
	Mass 3, Inguinal region/left, Small 1-1.9 cm	95-100
	Mass 4, Anogenital region, Small 1-1.9 cm	100

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - FEMALE

Group, Animal Number		Week(s) Sign Present
<u>1 mg/kg/day</u>		
1468	No Masses Detected	1-78
1469	No Masses Detected	1-100
1470	No Masses Detected	1-51
	Mass 1, Axillary region/right, Small 1-1.9 cm	52-62
	Mass 1, Axillary region/right, Ulcerated, small 1-1.9 cm	63
1471	No Masses Detected	1-100
1472	No Masses Detected	1-78
	Mass 1, Anogenital region, Medium 2-3.9 cm	85
	Mass 1, Anogenital region, Small 1-1.9 cm	79-84
1473	No Masses Detected	1-73
	Mass 1, Cervical region, Medium 2-3.9 cm	90-92
	Mass 1, Cervical region, Small 1-1.9 cm	74-89
	Mass 2, Axillary region/left, Small 1-1.9 cm	79-91
	Mass 2, Axillary region/left, Ulcerated, small 1-1.9 cm	92
1474	No Masses Detected	1-51
1475	No Masses Detected	1-85
	Mass 1, Anogenital region, Medium 2-3.9 cm	96-100
	Mass 1, Anogenital region, Small 1-1.9 cm	86-95

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - FEMALE

Group, Animal Number		Week(s) Sign Present
<u>1 mg/kg/day</u>		
1476	No Masses Detected	1-65, 77-85
	Mass 1, Anogenital region, Small 1-1.9 cm	66-76
	Mass 2, Anogenital region, Small 1-1.9 cm	86, 87
1477	No Masses Detected	1-86
1478	No Masses Detected	1-74
	Mass 1, Axillary region/left, Small 1-1.9 cm	75-90
	Mass 2, Axillary region/right, Small 1-1.9 cm	79-89
	Mass 2, Axillary region/right, Ulcerated, small 1-1.9 cm	90
1479	No Masses Detected	1-88
	Mass 1, Anogenital region, Small 1-1.9 cm	89
	Mass 1, Anogenital region, Ulcerated, small 1-1.9 cm	90
1480	No Masses Detected	1-77
<u>50 mg/kg/day</u>		
1481	No Masses Detected	1-52
1482	No Masses Detected	1-52
1483	No Masses Detected	1-52
1484	No Masses Detected	1-52

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - FEMALE

Group, Animal Number		Week(s) Sign Present
<u>50 mg/kg/day</u>		
1485	No Masses Detected	1-52
1486	No Masses Detected	1-52
1487	No Masses Detected	1-52
1488	No Masses Detected	1-50
	Mass 1, Inguinal region/right, Small 1-1.9 cm	51, 52
1489	No Masses Detected	1-52
1490	No Masses Detected	1-42
	Mass 1, Axillary region/right, Small 1-1.9 cm	43-52
1491	No Masses Detected	1-87
	Mass 1, Inguinal region/left, Small 1-1.9 cm	88-100
1492	No Masses Detected	1-73
1493	No Masses Detected	1-66
1494	No Masses Detected	1-100
1495	No Masses Detected	1-93
1496	No Masses Detected	1-100

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - FEMALE

Group, Animal Number		Week(s) Sign Present
<u>50 mg/kg/day</u>		
1497	No Masses Detected	1-47
	Mass 1, Inguinal region/left, Small 1-1.9 cm	48-56
1498	No Masses Detected	1-54
1499	No Masses Detected	1-59
	Mass 1, Cervical region, Large >or=4 cm	85-88
	Mass 1, Cervical region, Medium 2-3.9 cm	66-84
	Mass 1, Cervical region, Small 1-1.9 cm	60-65
	Mass 2, Axillary region/left, Large >or=4 cm	74-88
	Mass 2, Axillary region/left, Medium 2-3.9 cm	66-73
	Mass 2, Axillary region/left, Small 1-1.9 cm	60-65
1500	No Masses Detected	1-100
1501	No Masses Detected	1-61
1502	No Masses Detected	1-87
	Mass 1, Anogenital region, Small 1-1.9 cm	88-100
	Mass 2, Axillary region/right, Small 1-1.9 cm	95-99
	Mass 2, Axillary region/right, Ulcerated, small 1-1.9 cm	100
1503	No Masses Detected	1-91
1504	No Masses Detected	1-64

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - FEMALE

Group, Animal Number		Week(s) Sign Present
<u>50 mg/kg/day</u>		
1505	No Masses Detected	1-62
	Mass 1, Inguinal region/right, Large ≥ 4 cm	74-84
	Mass 1, Inguinal region/right, Medium 2-3.9 cm	66-73
	Mass 1, Inguinal region/right, Small 1-1.9 cm	63-65
	Mass 2, Cervical region, Small 1-1.9 cm	79-84
1506	No Masses Detected	1-36
	Mass 1, Thoracic region, Large ≥ 4 cm	60-62
	Mass 1, Thoracic region, Medium 2-3.9 cm	47-59
	Mass 1, Thoracic region, Small 1-1.9 cm	37-46
1507	No Masses Detected	1-60
1508	No Masses Detected	1-59
	Mass 1, Thoracic region, Large ≥ 4 cm	74-88
	Mass 1, Thoracic region, Medium 2-3.9 cm	66-73
	Mass 1, Thoracic region, Small 1-1.9 cm	60-65
1509	No Masses Detected	1-71
	Mass 1, Axillary region/right, Large ≥ 4 cm	85-92
	Mass 1, Axillary region/right, Medium 2-3.9 cm	79-84
	Mass 1, Axillary region/right, Small 1-1.9 cm	72-78
1510	No Masses Detected	1-67
1511	No Masses Detected	1-77

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - FEMALE

Group, Animal Number		Week(s) Sign Present
<u>50 mg/kg/day</u>		
1512	No Masses Detected	1-37
1513	No Masses Detected	1-40
1514	No Masses Detected	1-56
1515	No Masses Detected	1-33
	Mass 1, Cervical region, Large ≥ 4 cm	75
	Mass 1, Cervical region, Medium 2-3.9 cm	74
	Mass 1, Cervical region, Small 1-1.9 cm	34-73
	Mass 1, Cervical region, Ulcerated, large ≥ 4 cm	76
1516	No Masses Detected	1-99
	Mass 1, Axillary region/left, Small 1-1.9 cm	100
	Mass 2, Inguinal region/right, Small 1-1.9 cm	100
1517	No Masses Detected	1-66
	Mass 1, Cervical region, Medium 2-3.9 cm	74-78
	Mass 1, Cervical region, Small 1-1.9 cm	67-73
1518	No Masses Detected	1-19
	Mass 1, Axillary region/right, Small 1-1.9 cm	20-24
	Mass 1, Axillary region/right, Ulcerated, small 1-1.9 cm	25
1519	No Masses Detected	1-65

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - FEMALE

Group, Animal Number		Week(s) Sign Present
<u>50 mg/kg/day</u>		
1519	Mass 1, Axillary region/right, Small 1-1.9 cm	66-79
1520	No Masses Detected	1-100
1521	No Masses Detected	1-79
	Mass 1, Axillary region/right, Large ≥ 4 cm	85-87
	Mass 1, Axillary region/right, Medium 2-3.9 cm	82-84
	Mass 1, Axillary region/right, Small 1-1.9 cm	80, 81
	Mass 2, Inguinal region/right, Large ≥ 4 cm	85-87
	Mass 2, Inguinal region/right, Medium 2-3.9 cm	80-84
1522	No Masses Detected	1-67
	Mass 1, Anogenital region, Medium 2-3.9 cm	75-81
	Mass 1, Anogenital region, Small 1-1.9 cm	68-74
1523	No Masses Detected	1-83
	Mass 1, Axillary region/right, Small 1-1.9 cm	84-88
	Mass 2, Anogenital region, Medium 2-3.9 cm	88
1524	No Masses Detected	1-76
	Mass 1, Axillary region/left, Small 1-1.9 cm	77
	Mass 1, Axillary region/left, Ulcerated, small 1-1.9 cm	78
1525	No Masses Detected	1-74
1526	No Masses Detected	1-85

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - FEMALE

Group, Animal Number		Week(s) Sign Present
<u>50 mg/kg/day</u>		
1526	Mass 1, Abdominal region, Large ≥ 4 cm	91-95
	Mass 1, Abdominal region, Medium 2-3.9 cm	88-90
	Mass 1, Abdominal region, Small 1-1.9 cm	86, 87
1527	No Masses Detected	1-75
	Mass 1, Anogenital region, Large ≥ 4 cm	84-88
	Mass 1, Anogenital region, Medium 2-3.9 cm	76-83
	Mass 2, Axillary region/right, Small 1-1.9 cm	88
1528	No Masses Detected	1-85
	Mass 1, Inguinal region/right, Medium 2-3.9 cm	91-100
	Mass 1, Inguinal region/right, Small 1-1.9 cm	86-90
1529	No Masses Detected	1-63
1530	No Masses Detected	1-77
1531	No Masses Detected	1-85
1532	No Masses Detected	1-87
	Mass 1, Cervical region, Medium 2-3.9 cm	96-100
	Mass 1, Cervical region, Small 1-1.9 cm	88-95
1533	No Masses Detected	1-64
	Mass 1, Axillary region/left, Medium 2-3.9 cm	74-80

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - FEMALE

Group, Animal Number		Week(s) Sign Present
<u>50 mg/kg/day</u>		
1533	Mass 1, Axillary region/left, Small 1-1.9 cm	65-73
	Mass 1, Axillary region/left, Ulcerated, medium 2-3.9 cm	81
1534	No Masses Detected	1-83
1535	No Masses Detected	1-45
	Mass 1, Cervical region, Large ≥ 4 cm	66-74
	Mass 1, Cervical region, Medium 2-3.9 cm	60-65
	Mass 1, Cervical region, Small 1-1.9 cm	46-59
	Mass 1, Cervical region, Ulcerated, large ≥ 4 cm	75
1536	No Masses Detected	1-55
1537	No Masses Detected	1-81
1538	No Masses Detected	1-100
1539	No Masses Detected	1-67
	Mass 1, Axillary region/right, Medium 2-3.9 cm	74, 75
	Mass 1, Axillary region/right, Small 1-1.9 cm	68-73
1540	No Masses Detected	1-85
	Mass 1, Inguinal region/right, Small 1-1.9 cm	86-89
	Mass 1, Inguinal region/right, Ulcerated, medium 2-3.9 cm	90
	Mass 2, Thoracic region, Medium 2-3.9 cm	88-90

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - FEMALE

Group, Animal Number		Week(s) Sign Present
<u>50 mg/kg/day</u>		
1540	Mass 3, Axillary region/right, Medium 2-3.9 cm	88-90
	Mass 4, Axillary region/right, Small 1-1.9 cm	88-90
1541	No Masses Detected	1-100
1542	No Masses Detected	1-45
1543	No Masses Detected	1-100
1544	No Masses Detected	1-75
1545	No Masses Detected	1-47
1546	No Masses Detected	1-100
1547	No Masses Detected	1-100
1548	No Masses Detected	1-79
	Mass 1, Anogenital region, Large ≥ 4 cm	84-88
	Mass 1, Anogenital region, Medium 2-3.9 cm	80-83
1549	No Masses Detected	1-99
	Mass 1, Anogenital region, Small 1-1.9 cm	100
1550	No Masses Detected	1-85

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - FEMALE

Group, Animal Number		Week(s) Sign Present
<u>50 mg/kg/day</u>		
1550	Mass 1, Inguinal region/left, Small 1-1.9 cm	86-90
1551	No Masses Detected	1-67
1552	No Masses Detected	1-51
1553	No Masses Detected	1-99
	Mass 1, Inguinal region/right, Small 1-1.9 cm	100
1554	No Masses Detected	1-69
1555	No Masses Detected	1-46
1556	No Masses Detected	1-37
	Mass 1, Anogenital region, Small 1-1.9 cm	38-50
1557	No Masses Detected	1-94
1558	No Masses Detected	1-74
	Mass 1, Axillary region/left, Large ≥ 4 cm	85-88
	Mass 1, Axillary region/left, Medium 2-3.9 cm	82-84
	Mass 1, Axillary region/left, Small 1-1.9 cm	75-81
1559	No Masses Detected	1-87
	Mass 1, Inguinal region/right, Small 1-1.9 cm	88-100

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - FEMALE

Group, Animal Number		Week(s) Sign Present
<u>50 mg/kg/day</u>		
1560	No Masses Detected	1-53
	Mass 1, Cervical region, Medium 2-3.9 cm	66-79
	Mass 1, Cervical region, Small 1-1.9 cm	54-65
	Mass 1, Cervical region, Ulcerated, medium 2-3.9 cm	80, 81
<u>500 mg/kg/day</u>		
1561	No Masses Detected	1-52
1562	No Masses Detected	1-52
1563	No Masses Detected	1-52
1564	No Masses Detected	1-52
1565	No Masses Detected	1-52
1566	No Masses Detected	1-49
1567	No Masses Detected	1-49
1568	No Masses Detected	1-48
	Mass 1, Anogenital region, Small 1-1.9 cm	49-52
1569	No Masses Detected	1-51
	Mass 1, Anogenital region, Medium 2-3.9 cm	52

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - FEMALE

Group, Animal Number		Week(s) Sign Present
<u>500 mg/kg/day</u>		
1570	No Masses Detected	1-52
1571	No Masses Detected	1-52
1572	No Masses Detected	1-52
1573	No Masses Detected	1-91
	Mass 1, Abdominal region, Medium 2-3.9 cm	95-97
	Mass 1, Abdominal region, Small 1-1.9 cm	92-94
1574	No Masses Detected	1-73
1575	No Masses Detected	1-73
1576	No Masses Detected	1-85
	Mass 1, Inguinal region/left, Large ≥ 4 cm	95-100
	Mass 1, Inguinal region/left, Medium 2-3.9 cm	91-94
	Mass 1, Inguinal region/left, Small 1-1.9 cm	86-90
1577	No Masses Detected	1-81
	Mass 1, Anogenital region, Medium 2-3.9 cm	84-86
	Mass 1, Anogenital region, Small 1-1.9 cm	82, 83
	Mass 1, Anogenital region, Ulcerated, medium 2-3.9 cm	87
	Mass 2, Inguinal region/right, Small 1-1.9 cm	83-87
1578	No Masses Detected	1-100

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - FEMALE

Group, Animal Number		Week(s) Sign Present
<u>500 mg/kg/day</u>		
1579	No Masses Detected	1-65
	Mass 1, Axillary region/right, Medium 2-3.9 cm	83-87
	Mass 1, Axillary region/right, Small 1-1.9 cm	66-82
1580	No Masses Detected	1-50
1581	No Masses Detected	1-100
1582	No Masses Detected	1-89
1583 ^r	No Masses Detected	1-46
	Mass 1, Axillary region/right, Small 1-1.9 cm	47-56
	Mass 1, Axillary region/right, Ulcerated, small 1-1.9 cm	57
	Mass 2, Anogenital region, Small 1-1.9 cm	52-57
1584 ^r	No Masses Detected	1-76
1585	No Masses Detected	1-100
1586	No Masses Detected	1-84
1587	No Masses Detected	1-100
1588	No Masses Detected	1-51
	Mass 1, Axillary region/right, Large >or=4 cm	68-80

^r Replacement animal

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - FEMALE

Group, Animal Number		Week(s) Sign Present
<u>500 mg/kg/day</u>		
1588	Mass 1, Axillary region/right, Medium 2-3.9 cm	60-67
	Mass 1, Axillary region/right, Small 1-1.9 cm	52-59
	Mass 1, Axillary region/right, Ulcerated, large ≥ 4 cm	81
1589	No Masses Detected	1-80
1590	No Masses Detected	1-76
	Mass 1, Inguinal region/left, Medium 2-3.9 cm	83, 84
	Mass 1, Inguinal region/left, Small 1-1.9 cm	77-82
	Mass 1, Inguinal region/left, Ulcerated, medium 2-3.9 cm	85
1591	No Masses Detected	1-84
1592	No Masses Detected	1-86
	Mass 1, Inguinal region/left, Small 1-1.9 cm	87-89
	Mass 1, Inguinal region/left, Ulcerated, small 1-1.9 cm	90
1593	No Masses Detected	1-100
1594	No Masses Detected	1-100
1595	No Masses Detected	1-100
1596	No Masses Detected	1-55
1597	No Masses Detected	1-90

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - FEMALE

Group, Animal Number		Week(s) Sign Present
<u>500 mg/kg/day</u>		
1597	Mass 1, Abdominal region, Small 1-1.9 cm	91, 92
1598	No Masses Detected	1-84
1599	No Masses Detected	1-82
1600	No Masses Detected	1-66
	Mass 1, Cervical region, Large ≥ 4 cm	86-99
	Mass 1, Cervical region, Medium 2-3.9 cm	74-85
	Mass 1, Cervical region, Small 1-1.9 cm	67-73
	Mass 2, Axillary region/left, Medium 2-3.9 cm	96-99
	Mass 2, Axillary region/left, Small 1-1.9 cm	88-95
1601	No Masses Detected	1-67
	Mass 1, Inguinal region/left, Small 1-1.9 cm	68
1602	No Masses Detected	1-84
1603	No Masses Detected	1-51
	Mass 1, Anogenital region, Large ≥ 4 cm	86-88
	Mass 1, Anogenital region, Medium 2-3.9 cm	84, 85
	Mass 1, Anogenital region, Small 1-1.9 cm	52-83
	Mass 2, Cervical region, Medium 2-3.9 cm	84-88
	Mass 2, Cervical region, Small 1-1.9 cm	82, 83
1604	No Masses Detected	1-57

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - FEMALE

Group, Animal Number		Week(s) Sign Present
<u>500 mg/kg/day</u>		
1605	No Masses Detected	1-72
1606	No Masses Detected	1-51
	Mass 1, Inguinal region/right, Medium 2-3.9 cm	63-68
	Mass 1, Inguinal region/right, Small 1-1.9 cm	52-62
1607	No Masses Detected	1-100
1608	No Masses Detected	1-75
1609	No Masses Detected	1-95
	Mass 1, Anogenital region, Small 1-1.9 cm	96-98
1610	No Masses Detected	1-45
1611	No Masses Detected	1-85
	Mass 1, Inguinal region/left, Large ≥ 4 cm	88
	Mass 1, Inguinal region/left, Medium 2-3.9 cm	86, 87
1612	No Masses Detected	1-100
1613	No Masses Detected	1-87
	Mass 1, Inguinal region/left, Large ≥ 4 cm	96-100
	Mass 1, Inguinal region/left, Medium 2-3.9 cm	88-95
	Mass 2, Inguinal region/right, Medium 2-3.9 cm	99, 100

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - FEMALE

Group, Animal Number		Week(s) Sign Present
<u>500 mg/kg/day</u>		
1613	Mass 2, Inguinal region/right, Small 1-1.9 cm	92-98
1614	No Masses Detected	1-58
1615	No Masses Detected	1-78
1616	No Masses Detected	1-82
1617	No Masses Detected	1-57
1618	No Masses Detected	1-100
1619	No Masses Detected	1-81
	Mass 1, Axillary region/right, Large ≥ 4 cm	92-95
	Mass 1, Axillary region/right, Medium 2-3.9 cm	86-91
	Mass 1, Axillary region/right, Small 1-1.9 cm	82-85
	Mass 1, Axillary region/right, Ulcerated, large ≥ 4 cm	96
	Mass 2, Inguinal region/left, Medium 2-3.9 cm	96
	Mass 2, Inguinal region/left, Small 1-1.9 cm	86-95
1620	No Masses Detected	1-89
	Mass 1, Anogenital region, Ulcerated, medium 2-3.9 cm	90
1621	No Masses Detected	1-100
1622	No Masses Detected	1-95

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - FEMALE

Group, Animal Number		Week(s) Sign Present
<u>500 mg/kg/day</u>		
1623	No Masses Detected	1-100
1624	No Masses Detected	1-82
	Mass 1, Cervical region, Small 1-1.9 cm	83, 84
1625	No Masses Detected	1-82
1626	No Masses Detected	1-81
	Mass 1, Thoracic region, Small 1-1.9 cm	82, 83
	Mass 1, Thoracic region, Ulcerated, medium 2-3.9 cm	84
1627	No Masses Detected	1-48
	Mass 1, Axillary region/right, Small 1-1.9 cm	49-56
	Mass 1, Axillary region/right, Ulcerated, small 1-1.9 cm	57
1628	No Masses Detected	1-100
1629	No Masses Detected	1-90
1630	No Masses Detected	1-87
	Mass 1, Thoracic region, Small 1-1.9 cm	88-90
1631	No Masses Detected	1-100
1632	No Masses Detected	1-100

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - FEMALE

Group, Animal Number		Week(s) Sign Present
<u>500 mg/kg/day</u>		
1633	No Masses Detected	1-91
	Mass 1, Inguinal region/right, Small 1-1.9 cm	92-100
1634	No Masses Detected	1-62
	Mass 1, Anogenital region, Medium 2-3.9 cm	84-90
	Mass 1, Anogenital region, Small 1-1.9 cm	63-83
	Mass 2, Anogenital region, Medium 2-3.9 cm	88, 89
	Mass 2, Anogenital region, Ulcerated, medium 2-3.9 cm	90
1635	No Masses Detected	1-59
	Mass 1, Abdominal region, Large ≥ 4 cm	66
	Mass 1, Abdominal region, Medium 2-3.9 cm	63-65
	Mass 1, Abdominal region, Small 1-1.9 cm	60-62
1636	No Masses Detected	1-62
	Mass 1, Axillary region/left, Small 1-1.9 cm	63-77
	Mass 2, Inguinal region/left, Large ≥ 4 cm	74-76
	Mass 2, Inguinal region/left, Medium 2-3.9 cm	72, 73
	Mass 2, Inguinal region/left, Small 1-1.9 cm	63-71
	Mass 2, Inguinal region/left, Ulcerated, medium 2-3.9 cm	77
	Mass 3, Axillary region/right, Large ≥ 4 cm	74-77
	Mass 3, Axillary region/right, Small 1-1.9 cm	63-73
1637	No Masses Detected	1-81
	Mass 1, Inguinal region/right, Medium 2-3.9 cm	83-87

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Mass Findings - FEMALE

Group, Animal Number		Week(s) Sign Present
<u>500 mg/kg/day</u>		
1637	Mass 1, Inguinal region/right, Small 1-1.9 cm	82
1638	No Masses Detected	1-62
	Mass 1, Inguinal region/left, Medium 2-3.9 cm	72-95
	Mass 1, Inguinal region/left, Small 1-1.9 cm	63-71
	Mass 1, Inguinal region/left, Ulcerated, medium 2-3.9 cm	96
	Mass 2, Anogenital region, Medium 2-3.9 cm	90-96
1639	No Masses Detected	1-28
1640	No Masses Detected	1-87